



(19) World Intellectual Property Organization
International Bureau



(10) International Publication Number
WO 02/099122 A1

(43) International Publication Date
12 December 2002 (12.12.2002) PCT

(51) International Patent Classification¹: C12Q 1/00, 1/68, G01N 33/53, A61K 49/00 (74) Agents: BRUNELLE, Jan et al.; Exelixis, Inc., P.O. Box 511, 170 Harbor Way, South San Francisco, CA 94083-0511 (US).

(21) International Application Number: PCT/US02/17382

(22) International Filing Date: 3 June 2002 (03.06.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60296.076 5 June 2001 (05.06.2001) US
60328.605 10 October 2001 (10.10.2001) US
60357.253 15 February 2002 (15.02.2002) US

(71) Applicant (for all designated States except US): EX-ELIXIS, INC. (US/US); P.O. Box 511, 170 Harbor Way, South San Francisco, CA 94083-0511 (US).

(72) Inventors; and
(73) Inventors/Applicants (for US only): FRIEDMAN, Lori (US/US); One Bayview Village, Place, Unit 212, San Francisco, CA 94107 (US); PLOWMAN, Gregory, D. (US/US); 35 Winding Way, San Carlos, CA 94070 (US); BELVIN, Marela (US/US); 921 Santa Fe Avenue, Albany, CA 94706 (US); FRANCIS-LANG, Helen (GIB/US); 1782 Pacific Avenue, Apt. 2, San Francisco, CA 94109 (US); Li, Dexi (CN/US); 90 Behr Avenue, #302, San Francisco, CA 94131 (US); FUNK, Roel, P. (NL/US); 343 California Avenue, South San Francisco, CA 94080 (US).

Published:

— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MODIFIERS OF THE p53 PATHWAY AND METHODS OF USE

(57) Abstract: Human p53 genes are identified as modulators of the p53 pathway, and thus are therapeutic targets for disorders associated with defective p53 function. Methods for identifying modulators of p53, comprising screening for agents that modulate the activity of p53 are provided.

MODIFIERS OF THE p53 PATHWAY AND METHODS OF USE

REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. provisional patent applications 60/296,076 filed 6/5/2001, 60/328,605 filed 10/10/2001, and 60/357,253 filed 2/15/2002. The contents of the prior applications are hereby incorporated in their entirety.

BACKGROUND OF THE INVENTION

The p53 gene is mutated in over 50 different types of human cancers, including familial and spontaneous cancers, and is believed to be the most commonly mutated gene in human cancer (Zambetti and Levine, *FASEB* (1993) 7:855-865; Hollstein, *et al.*, *Nucleic Acids Res.* (1994) 22:3551-3555). Greater than 90% of mutations in the p53 gene are missense mutations that alter a single amino acid that inactivates p53 function. Aberrant forms of human p53 are associated with poor prognosis, more aggressive tumors, metastasis, and short survival rates (Mitsudomi *et al.*, *Clin Cancer Res* 2000 Oct; 6(10):4055-63; Koshland, *Science* (1993) 262:1953).

The human p53 protein normally functions as a central integrator of signals including DNA damage, hypoxia, nucleotide deprivation, and oncogene activation (Prives, *Cell* (1998) 95:5-8). In response to these signals, p53 protein levels are greatly increased with the result that the accumulated p53 activates cell cycle arrest or apoptosis depending on the nature and strength of these signals. Indeed, multiple lines of experimental evidence have pointed to a key role for p53 as a tumor suppressor (Levine, *Cell* (1997) 88:323-331). For example, homozygous p53 "knockout" mice are developmentally normal but exhibit nearly 100% incidence of neoplasia in the first year of life (Donchower *et al.*, *Nature* (1992) 356:215-221).

The biochemical mechanisms and pathways through which p53 functions in normal and cancerous cells are not fully understood, but one clearly important aspect of p53 function is its activity as a gene-specific transcriptional activator. Among the genes with known p53-response elements are several with well-characterized roles in either regulation of the cell cycle or apoptosis, including GADD45, p21/Waf1/Cip1, cyclin G, Bax, IGF-BP3, and MDM2 (Levine, *Cell* (1997) 88:323-331).

The ability to manipulate the genomes of model organisms such as *Drosophila* provides a powerful means to analyze biochemical processes that, due to significant evolutionary conservation, have direct relevance to more complex vertebrate organisms.

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The ability to manipulate the genomes of model organisms such as *Drosophila* provides a powerful means to analyze biochemical processes that, due to significant evolutionary conservation, have direct relevance to more complex vertebrate organisms.

Due to a high level of gene and pathway conservation, the strong similarity of cellular processes, and the functional conservation of genes between these model organisms and mammals, identification of the involvement of novel genes in particular pathways and their functions in such model organisms can directly contribute to the understanding of the correlative pathways and methods of modulating them in mammals (see, for example, Mechler *BM et al.*, 1985 *EMBO J* 4:1551-1557; Giatelli *E.* 1982 *Adv. Cancer Res.* 37: 33-74; Watson *KL, et al.*, 1994 *J Cell Sci.* 18: 19-33; Miklos *GL, and Rubin GM.* 1996 *Cell* 86:521-529; Wassarman *DA, et al.*, 1995 *Curr Opin Gen Dev* 5: 44-50; and Booth *DR.* 1999 *Cancer Metastasis Rev.* 18: 261-284). For example, a genetic screen can be carried out in an invertebrate model organism having underexpression (e.g. knockout) or overexpression of a gene (referred to as a "genetic entry point") that yields a visible phenotype. Additional genes are mutated in a random or targeted manner. When a gene mutation changes the original phenotype caused by the mutation in the genetic entry point, the gene is identified as a "modifier" involved in the same or overlapping pathway as the genetic entry point. When the genetic entry point is an ortholog of a human gene implicated in a disease pathway, such as p53, modifier genes can be identified that may be attractive candidate targets for novel therapeutics.

All references cited herein, including sequence information in referenced Genbank identifier numbers and website references, are incorporated herein in their entirety.

SUMMARY OF THE INVENTION

We have discovered genes that modify the p53 pathway in *Drosophila*, and identified their human orthologs, hereinafter referred to as HM. The invention provides methods for utilizing these p53 modifier genes and polypeptides to identify candidate therapeutic agents that can be used in the treatment of disorders associated with defective p53 function. Preferred HM-modulating agents specifically bind to HM polypeptides and restore p53 function. Other preferred HM-modulating agents are nucleic acid modulators such as antisense oligomers and RNAi that repress HM gene expression or product activity by, for example, binding to and inhibiting the respective nucleic acid (i.e. DNA or mRNA).

HM-specific modulating agents may be evaluated by any convenient *in vitro* or *in vivo* assay for molecular interaction with an HM polypeptide or nucleic acid. In one embodiment, candidate p53 modulating agents are tested with an assay system comprising a HM polypeptide or nucleic acid. Candidate agents that produce a change in the activity

of the assay system relative to controls are identified as candidate p53 modulating agents. The assay system may be cell-based or cell-free. HM-modulating agents include HM related proteins (e.g. dominant negative mutants, and biotherapeutics), HM-specific antibodies; HM-specific antisense oligomers and other nucleic acid modulators; and chemical agents that specifically bind HM or compete with HM binding target. In specific embodiments, the screening assay system is selected from a binding assay, an apoptosis assay, a cell proliferation assay, an angiogenesis assay, and a hypoxic induction assay.

In another embodiment, candidate p53 pathway modulating agents are further tested using a second assay system that detects changes in the p53 pathway, such as angiogenic, apoptotic, or cell proliferation changes produced by the originally identified candidate agent or an agent derived from the original agent. The second assay system may use cultured cells or non-human animals. In specific embodiments, the secondary assay system uses non-human animals, including animals predetermined to have a disease or disorder implicating the p53 pathway, such as an angiogenic, apoptotic, or cell proliferation disorder (e.g. cancer).

The invention further provides methods for modulating the p53 pathway in a mammalian cell by contacting the mammalian cell with an agent that specifically binds a HM polypeptide or nucleic acid. The agent may be a small molecule modulator, a nucleic acid modulator, or an antibody and may be administered to a mammalian animal predetermined to have a pathology associated the p53 pathway.

DETAILED DESCRIPTION OF THE INVENTION

Genetic screens were designed to identify modifiers of the p53 pathway in *Drosophila* in which p53 was overexpressed in the wing (Ollmann M, et al., Cell 2000 101: 91-101). Modifiers of the wing phenotype were identified as a modifier of the p53 pathway. Accordingly, vertebrate orthologs of these modifiers, and preferably the human orthologs, HM genes (i.e., nucleic acids and polypeptides) are attractive drug targets for the treatment of pathologies associated with a defective p53 signaling pathway, such as cancer. Table 1 lists the modifiers and their orthologs.

In vitro and in vivo methods of assessing HM function are provided herein. Modulation of the HM or their respective binding partners is useful for understanding the association of the p53 pathway and its members in normal and disease conditions and for developing diagnostics and therapeutic modalities for p53 related pathologies. HM-modulating agents that act by inhibiting or enhancing HM expression, directly or

indirectly, for example, by affecting an HM function such as enzymatic (e.g., catalytic) or binding activity, can be identified using methods provided herein. HM modulating agents are useful in diagnosis, therapy and pharmaceutical development.

5 Nucleic acids and polypeptides of the invention

Sequences related to HM nucleic acids and polypeptides that can be used in the invention are disclosed in Genbank (referenced by Genbank identifier (GI) number), shown in Table 1 and in the sequence listing.

A review of the nucleic acids and polypeptides of the invention reveals several categories of proteins, and their functional domains. Preferred HMs are enzymes or soluble proteins with ligand binding sites, including protein kinases, protein phosphatases, proteases, protease inhibitors, helicases, polymerases, prolysomerase, GTPase activating proteins (GAPs), guanine nucleotide exchange factors (GEFs), a range of metabolic enzymes, proteins involved in ubiquitination, DNA methylation and metabolism, RNA processing or binding, and adapters, among others. Alternative preferred targets are membrane proteins, such as G protein coupled receptors (GPCRs), protein kinase receptors, transporters, and ligand-gated ion channels, among others.

The term "HM polypeptide" refers to a full-length HM protein or a functionally active fragment or derivative thereof. A "functionally active" HM fragment or derivative exhibits one or more functional activities associated with a full-length, wild-type HM protein, such as antigenic or immunogenic activity, enzymatic activity, ability to bind natural cellular substrates, etc. The functional activity of HM proteins, derivatives and fragments can be assayed by various methods known to one skilled in the art (Current Protocols in Protein Science (1998) Coligan *et al.*, eds., John Wiley & Sons, Inc., Somerset, New Jersey) and as further discussed below. For purposes herein, functionally active fragments also include those fragments that comprise one or more structural domains of an HM, such as a kinase domain or a binding domain. Protein domains can be identified using the PFAM program (Bateman A., et al., Nucleic Acids Res, 1999, 27:260-2; <http://pfam.wustl.edu>). Methods for obtaining HM polypeptides are also further

described below. In some embodiments, preferred fragments are functionally active, domain-containing fragments comprising at least 25 contiguous amino acids, preferably at least 50, more preferably 75, and most preferably at least 100 contiguous amino acids of a domain-encoding region of an HM protein.

The term "HM nucleic acid" refers to a DNA or RNA molecule that encodes a HM polypeptide. Preferably, the HM polypeptide or nucleic acid or fragment thereof is from a human, but can also be an ortholog, or derivative thereof with at least 70% sequence identity, preferably at least 80%, more preferably 85%, still more preferably 90%, and most preferably at least 95% sequence identity with HM. Normally, orthologs in different species retain the same function, due to presence of one or more protein motifs and/or 3-dimensional structures. Orthologs are generally identified by sequence homology analysis, such as BLAST analysis, usually using protein bait sequences. Sequences are assigned as a potential ortholog if the best hit sequence from the forward BLAST result retrieves the original query sequence in the reverse BLAST (Huynen MA and Bork P, *Proc Natl Acad Sci* (1998) 95:5849-5856; Huynen MA *et al.*, *Genome Research* (2000) 10:1204-1210). Programs for multiple sequence alignment, such as CLUSTAL (Thompson JD *et al.*, 1994, *Nucleic Acids Res* 22:4673-4680) may be used to highlight conserved regions and/or residues of orthologous proteins and to generate phylogenetic trees. In a phylogenetic tree representing multiple homologous sequences from diverse species (e.g., retrieved through BLAST analysis), orthologous sequences from two species generally appear closest on the tree with respect to all other sequences from these two species. Structural threading or other analysis of protein folding (e.g., using software by ProCeryon, Biosciences, Salzburg, Austria) may also identify potential orthologs. In evolution, when a gene duplication event follows speciation, a single gene in one species, such as *Drosophila*, may correspond to multiple genes (paralogs) in another, such as human. As used herein, the term "orthologs" encompasses paralogs. As used herein, "percent (%) sequence identity" with respect to a subject sequence, or a specified portion of a subject sequence, is defined as the percentage of nucleotides or amino acids in the candidate derivative sequence identical with the nucleotides or amino acids in the subject sequence (or specified portion thereof), after aligning the sequences and introducing gaps, if necessary to achieve the maximum percent sequence identity, as generated by the program WU-BLAST-2.0a19 (Altschul *et al.*, *J. Mol. Biol.* (1997) 215:403-410; <http://blast.wustl.edu/blast/README.html>) with all the search parameters set to default values. The HSP S and HSP S2 parameters are dynamic values and are established by the program itself depending upon the composition of the particular sequence and composition of the particular database against which the sequence of interest is being searched. A % identity value is determined by the number of matching identical nucleotides or amino acids divided by the sequence length for which the percent identity is being reported.

"Percent (%) amino acid sequence similarity" is determined by doing the same calculation as for determining % amino acid sequence identity, but including conservative amino acid substitutions in addition to identical amino acids in the computation.

A conservative amino acid substitution is one in which an amino acid is substituted for another amino acid having similar properties such that the folding or activity of the protein is not significantly affected. Aromatic amino acids that can be substituted for each other are phenylalanine, tryptophan, and tyrosine; interchangeable hydrophobic amino acids are leucine, isoleucine, methionine, and valine; interchangeable polar amino acids are glutamine and asparagine; interchangeable basic amino acids are arginine, lysine and histidine; interchangeable acidic amino acids are aspartic acid and glutamic acid; and interchangeable small amino acids are alanine, serine, threonine, cysteine and glycine.

Alternatively, an alignment for nucleic acid sequences is provided by the local homology algorithm of Smith and Waterman (Smith and Waterman, 1981, *Advances in Applied Mathematics* 2:482-489; database: European Bioinformatics Institute <http://www.ebi.ac.uk/MParch/>; Smith and Waterman, 1981, *J. of Molec.Biol.*, 147:195-197; Nicholas *et al.*, 1998, "A Tutorial on Searching Sequence Databases and Sequence Scoring Methods" (www.psc.edu) and references cited therein.; W. R. Pearson, 1991, *Genomics* 11:635-650). This algorithm can be applied to amino acid sequences by using the scoring matrix developed by Dayhoff (Dayhoff: *Atlas of Protein Sequences and Structure*, M. O. Dayhoff *et al.*, 5 suppl. 3:353-358, National Biomedical Research Foundation, Washington, D.C., USA), and normalized by Gribskov (Gribskov 1986 *Nucl. Acids Res.* 14(6):6745-6763). The Smith-Waterman algorithm may be employed where default parameters are used for scoring (for example, gap open penalty of 12, gap extension penalty of two). From the data generated, the "Match" value reflects "sequence identity."

Derivative nucleic acid molecules of the subject nucleic acid molecules include sequences that hybridize to the nucleic acid sequence of an HM. The stringency of hybridization can be controlled by temperature, ionic strength, pH, and the presence of denaturing agents such as formamide during hybridization and washing. Conditions routinely used are set out in readily available procedure texts (e.g., *Current Protocol in Molecular Biology*, Vol. 1, Chap. 2.10, John Wiley & Sons, Publishers (1994); Sambrook *et al.*, *Molecular Cloning*, Cold Spring Harbor (1989)). In some embodiments, a nucleic acid molecule of the invention is capable of hybridizing to a nucleic acid molecule containing the nucleotide sequence of an HM under stringent hybridization conditions that

comprise: prehybridization of filters containing nucleic acid for 8 hours to overnight at 65° C in a solution comprising 6X single strength citrate (SSC) (1X SSC is 0.15 M NaCl, 0.015 M Na citrate; pH 7.0), 5X Denhardt's solution, 0.05% sodium pyrophosphate and 100 µg/ml herring sperm DNA; hybridization for 18-20 hours at 65° C in a solution containing 6X SSC, 1X Denhardt's solution, 100 µg/ml yeast tRNA and 0.05% sodium pyrophosphate; and washing of filters at 65° C for 1 h in a solution containing 0.2X SSC and 0.1% SDS (sodium dodecyl sulfate).

In other embodiments, moderately stringent hybridization conditions are used that comprise: pretreatment of filters containing nucleic acid for 6 h at 40° C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20h at 40° C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml salmon sperm DNA, and 10% (w/vol) dextran sulfate; followed by washing twice for 1 hour at 55° C in a solution containing 2X SSC and 0.1% SDS.

Alternatively, low stringency conditions can be used that comprise: incubation for 8 hours to overnight at 37° C in a solution comprising 20% formamide, 5 x SSC, 50 mM sodium phosphate (pH 7.6), 5X Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured sheared salmon sperm DNA; hybridization in the same buffer for 18 to 20 hours; and washing of filters in 1 x SSC at about 37° C for 1 hour.

Isolation, Production, Expression, and *in vivo* expression of HM Nucleic Acids and Polypeptides

HM nucleic acids and polypeptides, useful for identifying and testing agents that modulate HM function and for other applications related to the involvement of HM in the p53 pathway. HM nucleic acids and derivatives and orthologs thereof may be obtained using any available method. For instance, techniques for isolating cDNA or genomic DNA sequences of interest by screening DNA libraries or by using polymerase chain reaction (PCR) are well known in the art. In general, the particular use for the protein will dictate the particulars of expression, production, and purification methods. For instance, production of proteins for use in screening for modulating agents may require methods that preserve specific biological activities of these proteins, whereas production of proteins for antibody generation may require structural integrity of particular epitopes. Expression of proteins to be purified for screening or antibody production may require the addition of

specific tags (e.g., generation of fusion proteins). Overexpression of an HM protein for assays used to assess HM function, such as involvement in cell cycle regulation or hypoxic response, may require expression in eukaryotic cell lines capable of these cellular activities. Techniques for the expression, production, and purification of proteins are well known in the art: any suitable means therefore may be used (e.g., Higgins SJ and Hames BD (eds.) Protein Expression: A Practical Approach, Oxford University Press Inc., New York 1999; Stanbury PF et al., Principles of Fermentation Technology, 2nd edition, Elsevier Science, New York, 1995; Doonan S (ed.) Protein Purification Protocols, Humana Press, New Jersey, 1996; Coligan JE et al, Current Protocols in Protein Science (eds.), 1999, John Wiley & Sons, New York). In particular embodiments, recombinant HM is expressed in a cell line known to have defective p53 function (e.g. SAOS-2 osteoblasts, H1299 lung cancer cells, C33A and HT3 cervical cancer cells, HT-29 and DLD-1 colon cancer cells, among others, available from American Type Culture Collection (ATCC), Manassas, VA). The recombinant cells are used in cell-based screening assay systems of the invention, as described further below.

The nucleotide sequence encoding an HM polypeptide can be inserted into any appropriate expression vector. The necessary transcriptional and translational signals, including promoter/enhancer element, can derive from the native HM gene and/or its flanking regions or can be heterologous. A variety of host-vector expression systems may be utilized, such as mammalian cell systems infected with virus (e.g. vaccinia virus, adenovirus, etc.); insect cell systems infected with virus (e.g. baculovirus); microorganisms such as yeast containing yeast vectors, or bacteria transformed with bacteriophage, plasmid, or cosmid DNA. A host cell strain that modulates the expression of, modifies, and/or specifically processes the gene product may be used.

To detect expression of the HM gene product, the expression vector can comprise a promoter operably linked to an HM gene nucleic acid, one or more origins of replication, and, one or more selectable markers (e.g. thymidine kinase activity, resistance to antibiotics, etc.). Alternatively, recombinant expression vectors can be identified by assaying for the expression of the HM gene product based on the physical or functional properties of the HM protein in *in vitro* assay systems (e.g. immunoassays).

The HM protein, fragment, or derivative may be optionally expressed as a fusion, or chimeric protein product (i.e. it is joined via a peptide bond to a heterologous protein sequence of a different protein), for example to facilitate purification or detection. A chimeric product can be made by ligating the appropriate nucleic acid sequences encoding

the desired amino acid sequences to each other using standard methods and expressing the chimeric product. A chimeric product may also be made by protein synthetic techniques, e.g. by use of a peptide synthesizer (Hunkapiller *et al.*, Nature (1984) 310:105-111).

Once a recombinant cell that expresses the HM gene sequence is identified, the gene product can be isolated and purified using standard methods (e.g. ion exchange, affinity, and gel exclusion chromatography; centrifugation; differential solubility; electrophoresis, cite purification reference). Alternatively, native HM proteins can be purified from natural sources, by standard methods (e.g. immunoaffinity purification). Once a protein is obtained, it may be quantified and its activity measured by appropriate methods, such as immunoassay, bioassay, or other measurements of physical properties, such as crystallography.

The methods of this invention may also use cells that have been engineered for altered expression (mis-expression) of HM or other genes associated with the p53 pathway. As used herein, mis-expression encompasses ectopic expression, over-expression, under-expression, and non-expression (e.g. by gene knock-out or blocking expression that would otherwise normally occur).

Genetically modified animals

Animal models that have been genetically modified to alter HM expression may be used in *in vivo* assays to test for activity of a candidate p53 modulating agent, or to further assess the role of HM in a p53 pathway process such as apoptosis or cell proliferation.

Preferably, the altered HM expression results in a detectable phenotype, such as decreased or increased levels of cell proliferation, angiogenesis, or apoptosis compared to control animals having normal HM expression. The genetically modified animal may additionally have altered p53 expression (e.g. p53 knockout). Preferred genetically modified animals are mammals such as primates, rodents (preferably mice), cows, horses, goats, sheep, pigs, dogs and cats. Preferred non-mammalian species include zebrafish, *C. elegans*, and

Drosophila. Preferred genetically modified animals are transgenic animals having a heterologous nucleic acid sequence present as an extrachromosomal element in a portion of its cells, i.e. mosaic animals (see, for example, techniques described by Jakobovits, 1994, Curr. Biol. 4:761-763.) or stably integrated into its germ line DNA (i.e., in the genomic sequence of most or all of its cells). Heterologous nucleic acid is introduced into the germ line of such transgenic animals by genetic manipulation of, for example, embryos or embryonic stem cells of the host animal.

Methods of making transgenic animals are well-known in the art (for transgenic mice see Brinster *et al.*, Proc. Nat. Acad. Sci. USA 82: 4438-4442 (1985), U.S. Pat. Nos.

4,736,866 and 4,870,009, both by Leder *et al.*, U.S. Pat. No. 4,873,191 by Wagner *et al.*, and Hogan, B., Manipulating the Mouse Embryo, Cold Spring Harbor Laboratory Press,

5 Cold Spring Harbor, N.Y., (1986); for particle bombardment see U.S. Pat. No., 4,945,050, by Sandford *et al.*; for transgenic *Drosophila* see Rubin and Spradling, Science (1982) 218:348-53 and U.S. Pat. No. 4,670,388; for transgenic insects see Berghammer A.J. *et al.*, A Universal Marker for Transgenic Insects (1999) Nature 402:370-371; for transgenic Zebrafish see Lin S., Transgenic Zebrafish, Methods Mol Biol. (2000); 136:375-3830; for

10 microinjection procedures for fish, amphibian eggs and birds see Houdebine and Chourout, Experientia (1991) 47:897-905; for transgenic rats see Hammer *et al.*, Cell (1990) 63:1099-1112; and for culturing of embryonic stem (ES) cells and the subsequent production of transgenic animals by the introduction of DNA into ES cells using methods such as electroporation, calcium phosphate/DNA precipitation and direct injection see, e.g., Teratocarcinomas and Embryonic Stem Cells, A Practical Approach, E. J. Robertson, ed., IRL Press (1987). Clones of the nonhuman transgenic animals can be produced according to available methods (see Wilmut, I. *et al.* (1997) Nature 385:810-813; and PCT International Publication Nos. WO 97/07668 and WO 97/07669).

In one embodiment, the transgenic animal is a "knock-out" animal having a heterozygous or homozygous alteration in the sequence of an endogenous HM gene that results in a decrease of HM function, preferably such that HM expression is undetectable or insignificant. Knock-out animals are typically generated by homologous recombination with a vector comprising a transgene having at least a portion of the gene to be knocked out. Typically a deletion, addition or substitution has been introduced into the transgene to functionally disrupt it. The transgene can be a human gene (e.g., from a human genomic clone) but more preferably is an ortholog of the human gene derived from the transgenic host species. For example, a mouse HM gene is used to construct a homologous recombination vector suitable for altering an endogenous HM gene in the mouse genome. Detailed methodologies for homologous recombination in mice are available (see Capecchi, Science (1989) 244:1288-1292; Joyner *et al.*, Nature (1989) 338:153-156). Procedures for the production of non-rodent transgenic mammals and other

20 animals are also available (Houdebine and Chourout, *supra*; Pursel *et al.*, Science (1989) 244:1281-1288; Simms *et al.*, BioTechnology (1988) 6:179-183). In a preferred embodiment, knock-out animals, such as mice harboring a knockout of a specific gene,

may be used to produce antibodies against the human counterpart of the gene that has been knocked out (Claesson MH et al., (1994) *Scan J Immunol* 40:257-264; Declerck PJ et al., (1995) *J Biol Chem.* 270:8397-400).

In another embodiment, the transgenic animal is a "knock-in" animal having an alteration in its genome that results in altered expression (e.g., increased (including ectopic) or decreased expression) of the HM gene, e.g., by introduction of additional copies of HM, or by operatively inserting a regulatory sequence that provides for altered expression of an endogenous copy of the HM gene. Such regulatory sequences include inducible, tissue-specific, and constitutive promoters and enhancer elements. The knock-in can be homozygous or heterozygous.

Transgenic nonhuman animals can also be produced that contain selected systems allowing for regulated expression of the transgene. One example of such a system that may be produced is the cre/loxP recombinase system of bacteriophage P1 (Lakso et al., PNAS (1992) 89:6232-6236; U.S. Pat. No. 4,959,317). If a cre/loxP recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, e.g., by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase. Another example of a recombinase system is the Flp recombinase system of *Saccharomyces cerevisiae* (O'Gorman et al. (1991) *Science* 251:1351-1355; U.S. Pat. No. 5,654,182). In a preferred embodiment, both Cre-LoxP and Flp-Frt are used in the same system to regulate expression of the transgene, and for sequential deletion of vector sequences in the same cell (Sun X et al (2000) *Nat Genet* 25:83-6).

The genetically modified animals can be used in genetic studies to further elucidate the p53 pathway, as animal models of disease and disorders implicating defective p53 function, and for *in vivo* testing of candidate therapeutic agents, such as those identified in screens described below. The candidate therapeutic agents are administered to a genetically modified animal having altered HM function and phenotypic changes are compared with appropriate control animals such as genetically modified animals that receive placebo treatment, and/or animals with unaltered HM expression that receive candidate therapeutic agent.

In addition to the above-described genetically modified animals having altered HM function, animal models having defective p53 function (and otherwise normal HM

function), can be used in the methods of the present invention. For example, a p53 knockout mouse can be used to assess, *in vivo*, the activity of a candidate p53 modulating agent identified in one of the *in vitro* assays described below. p53 knockout mice are described in the literature (Jacks et al., *Nature* 2001;410:1111-1116, 1043-1044; Donchower et al., *supra*). Preferably, the candidate p53 modulating agent when administered to a model system with cells defective in p53 function, produces a detectable phenotypic change in the model system indicating that the p53 function is restored, i.e., the cells exhibit normal cell cycle progression.

10 Modulating Agents

The invention provides methods to identify agents that interact with and/or modulate the function of HM and/or the p53 pathway. Such agents are useful in a variety of diagnostic and therapeutic applications associated with the p53 pathway, as well as in further analysis of the HM protein and its contribution to the p53 pathway. Accordingly, the invention also provides methods for modulating the p53 pathway comprising the step of specifically modulating HM activity by administering a HM-interacting or -modulating agent.

In a preferred embodiment, HM-modulating agents inhibit or enhance HM activity or otherwise affect normal HM function, including transcription, protein expression, protein localization, and cellular or extra-cellular activity. In a further preferred embodiment, the candidate p53 pathway-modulating agent specifically modulates the function of the HM. The phrases "specific modulating agent", "specifically modulates", etc., are used herein to refer to modulating agents that directly bind to the HM polypeptide or nucleic acid, and preferably inhibit, enhance, or otherwise alter, the function of the HM. The term also encompasses modulating agents that alter the interaction of the HM with a binding partner or substrate (e.g. by binding to a binding partner of an HM, or to a protein/binding partner complex, and inhibiting function).

Preferred HM-modulating agents include small molecule compounds; HM-interacting proteins, including antibodies and other biotherapeutics; and nucleic acid modulators such as antisense and RNA inhibitors. The modulating agents may be formulated in pharmaceutical compositions, for example, as compositions that may comprise other active ingredients, as in combination therapy, and/or suitable carriers or excipients. Techniques for formulation and administration of the compounds may be found in "Remington's Pharmaceutical Sciences" Mack Publishing Co., Easton, PA, 19th edition.

Small molecule modulators

Small molecule modulators are preferred where the identified HM has enzymatic function, and/or contains protein interaction domains. Such HMs are represented, for example, in rows 1-23, 26-29, 33-35, 37, 43-66, and 70-115 of Table 1.

Small molecules are often preferred to modulate function of proteins with enzymatic function, and/or containing protein interaction domains. Chemical agents, referred to in the art as "small molecule" compounds are typically organic, non-peptide molecules, having a molecular weight less than 10,000, preferably less than 5,000, more preferably less than 1,000, and most preferably less than 500. This class of modulators includes chemically synthesized molecules, for instance, compounds from combinatorial chemical libraries. Synthetic compounds may be rationally designed or identified based on known or inferred properties of the HM protein or may be identified by screening compound libraries. Alternative appropriate modulators of this class are natural products, particularly secondary metabolites from organisms such as plants or fungi, which can also be identified by screening compound libraries for HM-modulating activity. Methods for generating and obtaining compounds are well known in the art (Schreiber SL, Science (2000) 151: 1964-1969; Radmann J and Gunther J, Science (2000) 151: 1947-1948).

Small molecule modulators identified from screening assays, as described below, can be used as lead compounds from which candidate clinical compounds may be designed, optimized, and synthesized. Such clinical compounds may have utility in treating pathologies associated with the p53 pathway. The activity of candidate small molecule modulating agents may be improved several-fold through iterative secondary functional validation, as further described below, structure determination, and candidate modulator modification and testing. Additionally, candidate clinical compounds are generated with specific regard to clinical and pharmacological properties. For example, the reagents may be derivatized and re-screened using *in vitro* and *in vivo* assays to optimize activity and minimize toxicity for pharmaceutical development.

Protein Modulators

Specific HM-interacting proteins are useful in a variety of diagnostic and therapeutic applications related to the p53 pathway and related disorders, as well as in validation assays for other HM-modulating agents. In a preferred embodiment, HM-interacting proteins affect normal HM function, including transcription, protein expression, protein localization, and cellular or extra-cellular activity. In another embodiment, HM-

interacting proteins are useful in detecting and providing information about the function of HM proteins, as is relevant to p53 related disorders, such as cancer (e.g., for diagnostic means).

An HM-interacting protein may be endogenous, i.e. one that naturally interacts genetically or biochemically with an HM, such as a member of the HM pathway that modulates HM expression, localization, and/or activity. HM-modulators include dominant negative forms of HM-interacting proteins and of HM proteins themselves. Yeast two-hybrid and variant screens offer preferred methods for identifying endogenous HM-interacting proteins (Finley, R. L. et al. (1996) in DNA Cloning-Expression Systems: A Practical Approach, eds. Glover D. & Hames B. D (Oxford University Press, Oxford, England), pp. 169-203; Fashema SF et al., Gene (2000) 250:1-14; Drees BL Curr Opin Chem Biol (1999) 3:64-70; Vidal M and Legrain P Nucleic Acids Res (1999) 27:919-29; and U.S. Pat. No. 5,928,868). Mass spectrometry is an alternative preferred method for the elucidation of protein complexes (reviewed in, e.g., Pandley A and Mann M, Nature (2000) 405:837-846; Yates JR 3rd, Trends Genet (2000) 16:5-8).

An HM-interacting protein may be an exogenous protein, such as an HM-specific antibody or a T-cell antigen receptor (see, e.g., Harlow and Lane (1988) Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory; Harlow and Lane (1999) Using antibodies: a laboratory manual. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press). HM antibodies are further discussed below.

In preferred embodiments, an HM-interacting protein specifically binds an HM protein. In alternative preferred embodiments, an HM-modulating agent binds an HM substrate, binding partner, or cofactor.

Antibodies

In another embodiment, the protein modulator is an HM specific antibody agonist or antagonist. While antibodies may be produced against any protein to dissect cellular processes, preferred HM candidates for antibody production for therapeutic applications include cell surface proteins, proteins with transmembrane domains, proteins with extracellular Ig or fibronectin domains, or proteins with no cytoplasmic retention domains. Such HM proteins are found, for example, in rows 22-23, 29, 36, 38-39, 41-42, 62, 65-69, 76, 79, 85-87, 95, and 103-107 of Table 1.

The antibodies have therapeutic and diagnostic utilities, and can be used in screening assays to identify HM modulators. The antibodies can also be used in dissecting the

portions of the HM pathway responsible for various cellular responses and in the general processing and maturation of the HM.

Antibodies that specifically bind HM polypeptides can be generated using known methods. Preferably the antibody is specific to a mammalian ortholog of HM polypeptide, and more preferably, to human HM. Antibodies may be polyclonal, monoclonal (mAbs), humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab')₂ subunits, fragments produced by a FAb expression library, anti-idiotypic (anti-Id) antibodies, and epitope-binding fragments of any of the above. Epitopes of HM which are particularly antigenic can be selected, for example, by routine screening of HM

polypeptides for antigenicity or by applying a theoretical method for selecting antigenic regions of a protein (Hopp and Wood (1981), *Proc. Natl. Acad. Sci. U.S.A.* 78:3824-28; Hopp and Wood, (1983) *Mol. Immunol.* 20:483-89; Sutcliffe et al., (1983) *Science* 219:660-66) to the amino acid sequence of an HM. Monoclonal antibodies with affinities of 10^8 M⁻¹ preferably 10^9 M⁻¹ to 10^{10} M⁻¹, or stronger can be made by standard procedures as described (Harlow and Lane, *supra*; Goding (1986) *Monoclonal Antibodies: Principles and Practice* (2d ed) Academic Press, New York; and U.S. Pat. Nos. 4,381,292; 4,451,570; and 4,618,577). Antibodies may be generated against crude cell extracts of HM or substantially purified fragments thereof. If HM fragments are used, they preferably comprise at least 10, and more preferably, at least 20 contiguous amino acids of an HM protein. In a particular embodiment, HM-specific antigens and/or immunogens are coupled to carrier proteins that stimulate the immune response. For example, the subject polypeptides are covalently coupled to the keyhole limpet hemocyanin (KLH) carrier, and the conjugate is emulsified in Freund's complete adjuvant, which enhances the immune response. An appropriate immune system such as a laboratory rabbit or mouse is immunized according to conventional protocols.

The presence of HM-specific antibodies is assayed by an appropriate assay such as a solid phase enzyme-linked immunosorbent assay (ELISA) using immobilized corresponding HM polypeptides. Other assays, such as radioimmunoassays or fluorescent assays might also be used.

Chimeric antibodies specific to HM polypeptides can be made that contain different portions from different animal species. For instance, a human immunoglobulin constant region may be linked to a variable region of a murine mAb, such that the antibody derives its biological activity from the human antibody, and its binding specificity from the murine fragment. Chimeric antibodies are produced by splicing together genes that

encode the appropriate regions from each species (Morrison et al., *Proc. Natl. Acad. Sci.* (1984) 81:6851-6855; Neuberger et al., *Nature* (1984) 312:604-608; Takeda et al., *Nature* (1985) 31:452-454). Humanized antibodies, which are a form of chimeric antibodies, can be generated by grafting complementary-determining regions (CDRs) (Carlos, T. M., J. M. Harlan, 1994, *Blood* 84:2068-2101) of mouse antibodies into a background of human framework regions and constant regions by recombinant DNA technology (Riechmann LM, et al., 1988 *Nature* 323: 323-327). Humanized antibodies contain ~10% murine sequences and ~90% human sequences, and thus further reduce or eliminate immunogenicity, while retaining the antibody specificities (Co MS, and Queen C. 1991 *Nature* 351: 501-501; Morrison SL, 1992 *Ann. Rev. Immun.* 10:239-265). Humanized antibodies and methods of their production are well-known in the art (U.S. Pat. Nos. 5,530,101, 5,585,089, 5,693,762, and 6,180,370).

HM-specific single chain antibodies which are recombinant, single chain polypeptides formed by linking the heavy and light chain fragments of the Fv regions via an amino acid bridge, can be produced by methods known in the art (U.S. Pat. No. 4,946,778; Bird, Science (1988) 242:423-426; Huston et al., *Proc. Natl. Acad. Sci. USA* (1988) 85:5879-5883; and Ward et al., *Nature* (1989) 334:544-546).

Other suitable techniques for antibody production involve in vitro exposure of lymphocytes to the antigenic polypeptides or alternatively to selection of libraries of antibodies in phage or similar vectors (Huse et al., *Science* (1989) 246:1275-1281). As used herein, T-cell antigen receptors are included within the scope of antibody modulators (Harlow and Lane, 1988, *supra*).

The polypeptides and antibodies of the present invention may be used with or without modification. Frequently, antibodies will be labeled by joining, either covalently or non-covalently, a substance that provides for a detectable signal, or that is toxic to cells that express the targeted protein (Menard S, et al., *Int. J. Biol. Markers* (1989) 4:131-134). A wide variety of labels and conjugation techniques are known and are reported extensively in both the scientific and patent literature. Suitable labels include radionuclides, enzymes, substrates, cofactors, inhibitors, fluorescent moieties, fluorescent emitting lanthanide metals, chemiluminescent moieties, bioluminescent moieties, magnetic particles, and the like (U.S. Pat. Nos. 3,817,837; 3,850,752; 3,939,350; 3,996,345; 4,277,437; 4,275,149; and 4,366,241). Also, recombinant immunoglobulins may be produced (U.S. Pat. No. 4,816,567). Antibodies to cytoplasmic polypeptides may be delivered and reach their

targets by conjugation with membrane-penetrating toxin proteins (U.S. Pat. No. 6,086,900).

When used therapeutically in a patient, the antibodies of the subject invention are typically administered parenterally, when possible at the target site, or intravenously. The therapeutically effective dose and dosage regimen is determined by clinical studies. Typically, the amount of antibody administered is in the range of about 0.1 mg/kg to about 10 mg/kg of patient weight. For parenteral administration, the antibodies are formulated in a unit dosage injectable form (e.g., solution, suspension, emulsion) in association with a pharmaceutically acceptable vehicle. Such vehicles are inherently nontoxic and non-therapeutic. Examples are water, saline, Ringer's solution, dextrose solution, and 5% human serum albumin. Nonaqueous vehicles such as fixed oils, ethyl oleate, or liposome carriers may also be used. The vehicle may contain minor amounts of additives, such as buffers and preservatives, which enhance isotonicity and chemical stability or otherwise enhance therapeutic potential. The antibodies' concentrations in such vehicles are typically in the range of about 1 mg/ml to about 10 mg/ml.

Immunotherapeutic methods are further described in the literature (US Pat. No. 5,859,206; WO0073469).

Specific biotherapeutics

In a preferred embodiment, an HM-interacting protein may have biotherapeutic applications. Biotherapeutic agents formulated in pharmaceutically acceptable carriers and dosages may be used to activate or inhibit signal transduction pathways. This modulation may be accomplished by binding a ligand, thus inhibiting the activity of the pathway; or by binding a receptor, either to inhibit activation of, or to activate, the receptor. Alternatively, the biotherapeutic may itself be a ligand capable of activating or inhibiting a receptor. Biotherapeutic agents and methods of producing them are described in detail in U.S. Pat. No. 6,146,628.

When the HM is a ligand, it may be used as a biotherapeutic agent to activate or inhibit its natural receptor. Alternatively, antibodies against HM, as described in the previous section, may be used as biotherapeutic agents.

When the HM is a receptor, its ligand(s), antibodies to the ligand(s) or the HM itself may be used as biotherapeutics to modulate the activity of HM in the p53 pathway.

Nucleic Acid Modulators

Other preferred HM-modulating agents comprise nucleic acid molecules, such as antisense oligomers or double stranded RNA (dsRNA), which generally inhibit HM activity. Preferred nucleic acid modulators interfere with the function of the HM nucleic acid such as DNA replication, transcription, translocation of the HM RNA to the site of protein translation, translation of protein from the HM RNA, splicing of the HM RNA to yield one or more mRNA species, or catalytic activity which may be engaged in or facilitated by the HM RNA. All HM proteins may be targeted by nucleic acid modulators, but preferred targets include transcription factors and cytoplasmic proteins. Thus, all HMs on Table 1, for example, can be targets for nucleic acid modulators.

In one embodiment, the antisense oligomer is an oligonucleotide that is sufficiently complementary to an HM mRNA to bind to and prevent translation, preferably by binding to the 5' untranslated region. HM-specific antisense oligonucleotides, preferably range from at least 6 to about 200 nucleotides. In some embodiments the oligonucleotide is preferably at least 10, 15, or 20 nucleotides in length. In other embodiments, the oligonucleotide is preferably less than 50, 40, or 30 nucleotides in length. The oligonucleotide can be DNA or RNA or a chimeric mixture or derivatives or modified versions thereof, single-stranded or double-stranded. The oligonucleotide can be modified at the base moiety, sugar moiety, or phosphate backbone. The oligonucleotide may include other appending groups such as peptides, agents that facilitate transport across the cell membrane, hybridization-triggered cleavage agents, and intercalating agents.

In another embodiment, the antisense oligomer is a phosphothioate morpholino oligomer (PMO). PMOs are assembled from four different morpholino subunits, each of which contain one of four genetic bases (A, C, G, or T) linked to a six-membered morpholine ring. Polymers of these subunits are joined by non-ionic phosphodiarnidate intersubunit linkages. Details of how to make and use PMOs and other antisense oligomers are well known in the art (e.g. see WO99/18193; Probst JC, Antisense Oligodeoxynucleotide and Ribozyme Design, Methods (2000) 22(3):271-281; Summerton J, and Weller D. 1997 Antisense Nucleic Acid Drug Dev. 7:187-95; US Pat. No. 5,235,033; and US Pat No. 5,378,841).

Alternative preferred HM nucleic acid modulators are double-stranded RNA species mediating RNA interference (RNAi). RNAi is the process of sequence-specific, post-transcriptional gene silencing in animals and plants, initiated by double-stranded RNA (dsRNA) that is homologous in sequence to the silenced gene. Methods relating to the use

of RNAi to silence genes in *C. elegans*, *Drosophila*, plants, and humans are known in the art (Fire A, et al., 1998 Nature 391:806-811; Fire, A. Trends Genet. 15, 358-363 (1999); Sharp, P. A. RNA interference 2001. Genes Dev. 15, 485-490 (2001); Hammond, S. M., et al., Nature Rev. Genet. 2, 110-1119 (2001); Tuschl, T. Chem. Biochem. 2, 239-245 (2001); Hamilton, A. et al., Science 286, 950-952 (1999); Hammond, S. M., et al., Nature 404, 293-296 (2000); Zamore, P. D., et al., Cell 101, 25-33 (2000); Bernstein, E., et al., Nature 409, 363-366 (2001); Elbashir, S. M., et al., Genes Dev. 15, 188-200 (2001); WO0129058; WO9932619; Elbashir SM, et al., 2001 Nature 411:494-498).

Nucleic acid modulators are commonly used as research reagents, diagnostics, and therapeutics. For example, antisense oligonucleotides, which are able to inhibit gene expression with exquisite specificity, are often used to elucidate the function of particular genes (see, for example, U.S. Pat. No. 6,165,790). Nucleic acid modulators are also used, for example, to distinguish between functions of various members of a biological pathway. For example, antisense oligomers have been employed as therapeutic moieties in the treatment of disease states in animals and man and have been demonstrated in numerous clinical trials to be safe and effective (Milligan JP, et al, Current Concepts in Antisense Drug Design, J Med Chem. (1993) 36:1923-1937; Tonkinson JL et al., Antisense Oligodeoxynucleotides as Clinical Therapeutic Agents, Cancer Invest. (1996) 14:34-65). Accordingly, in one aspect of the invention, an HM-specific nucleic acid modulator is used in an assay to further elucidate the role of the HM in the p53 pathway, and/or its relationship to other members of the pathway. In another aspect of the invention, an HM-specific antisense oligomer is used as a therapeutic agent for treatment of p53-related disease states.

25 Assay Systems

The invention provides assay systems and screening methods for identifying specific modulators of HM activity. As used herein, an "assay system" encompasses all the components required for performing and analyzing results of an assay that detects and/or measures a particular event. In general, primary assays are used to identify or confirm a modulator's specific biochemical or molecular effect with respect to the HM nucleic acid or protein. In general, secondary assays further assess the activity of a HM modulating agent identified by a primary assay and may confirm that the modulating agent affects HM in a manner relevant to the p53 pathway. In some cases, HM modulators will be directly tested in a secondary assay.

In a preferred embodiment, the screening method comprises contacting a suitable assay system comprising an HM polypeptide with a candidate agent under conditions whereby, but for the presence of the agent, the system provides a reference activity (e.g. kinase activity), which is based on the particular molecular event the screening method detects. A statistically significant difference between the agent-biased activity and the reference activity indicates that the candidate agent modulates HM activity, and hence the p53 pathway.

Primary Assays

10 The type of modulator tested generally determines the type of primary assay.

Primary assays for small molecule modulators

For small molecule modulators, screening assays are used to identify candidate modulators. Screening assays may be cell-based or may use a cell-free system that recreates or retains the relevant biochemical reaction of the target protein (reviewed in Sittampalam GS et al., Curr Opin Chem Biol (1997) 1:384-91 and accompanying references). As used herein the term "cell-based" refers to assays using live cells, dead cells, or a particular cellular fraction, such as a membrane, endoplasmic reticulum, or mitochondrial fraction. The term "cell free" encompasses assays using substantially purified protein (either endogenous or recombinantly produced), partially purified or crude cellular extracts. Screening assays may detect a variety of molecular events, including protein-DNA interactions, protein-protein interactions (e.g., receptor-ligand binding), transcriptional activity (e.g., using a reporter gene), enzymatic activity (e.g., via a property of the substrate), activity of second messengers, immunogenicity and changes in cellular morphology or other cellular characteristics. Appropriate screening assays may use a wide range of detection methods including fluorescent, radioactive, colorimetric, spectrophotometric, and amperometric methods, to provide a read-out for the particular molecular event detected.

Cell-based screening assays usually require systems for recombinant expression of HM and any auxiliary proteins demanded by the particular assay. Appropriate methods for generating recombinant proteins produce sufficient quantities of proteins that retain their relevant biological activities and are of sufficient purity to optimize activity and assure assay reproducibility. Yeast two-hybrid and variant screens, and mass spectrometry provide preferred methods for determining protein-protein interactions and elucidation of

protein complexes. In certain applications, when HM-interacting proteins are used in screens to identify small molecule modulators, the binding specificity of the interacting protein to the HM protein may be assayed by various known methods such as substrate processing (e.g. ability of the candidate HM-specific binding agents to function as negative effectors in HM-expressing cells), binding equilibrium constants (usually at least about $10^7 M^{-1}$, preferably at least about $10^8 M^{-1}$, more preferably at least about $10^9 M^{-1}$), and immunogenicity (e.g. ability to elicit HM specific antibody in a heterologous host such as a mouse, rat, goat or rabbit). For enzymes and receptors, binding may be assayed by, respectively, substrate and ligand processing.

The screening assay may measure a candidate agent's ability to specifically bind to or modulate activity of a HM polypeptide, a fusion protein thereof, or to cells or membranes bearing the polypeptide or fusion protein. The HM polypeptide can be full length or a fragment thereof that retains functional HM activity. The HM polypeptide may be fused to another polypeptide, such as a peptide tag for detection or anchoring, or to another tag. The HM polypeptide is preferably human HM, or is an ortholog or derivative thereof as described above. In a preferred embodiment, the screening assay detects candidate agent-based modulation of HM interaction with a binding target, such as an endogenous or exogenous protein or other substrate that has HM-specific binding activity, and can be used to assess normal HM gene function.

Suitable assay formats that may be adapted to screen for HM modulators are known in the art. Preferred screening assays are high throughput or ultra high throughput and thus provide automated, cost-effective means of screening compound libraries for lead compounds (Fernandes PB, *Curr Opin Chem Biol* (1998) 2:597-603; Sundberg SA, *Curr Opin Biotechnol* 2000, 11:47-53). In one preferred embodiment, screening assays uses fluorescence technologies, including fluorescence polarization, time-resolved fluorescence, and fluorescence resonance energy transfer. These systems offer means to monitor protein-protein or DNA-protein interactions in which the intensity of the signal emitted from dye-labeled molecules depends upon their interactions with partner molecules (e.g., Selvin PR, *Nat Struct Biol* (2000) 7:730-4; Fernandes PB, *supra*; Hertzberg RP and Pope AJ, *Curr Opin Chem Biol* (2000) 4:445-451).

A variety of suitable assay systems may be used to identify candidate HM and p53 pathway modulators (e.g. U.S. Pat. No. 6,165,992 (kinase assays); U.S. Pat. Nos. 5,550,019 and 6,133,437 (apoptosis assays); U.S. Pat. No. 6,020,135 (p53 modulation),

WO 01/25487 (Helicase assays), U.S. Pat. No. 6,114,132 (phosphatase and protease assays), among others). Specific preferred assays are described in more detail below.

As seen from Table 1, preferred HMs are enzymes or soluble proteins with ligand binding sites, including protein kinases, protein phosphatases, proteases, protease inhibitors, helicases, polymerases, prolylisoamerses, hydrolases, reductases, GTPase activating proteins (GAPs), guanine nucleotide exchange factors (GEFs), a range of metabolic enzymes, proteins involved in ubiquitination, DNA methylation and metabolism, RNA processing or binding, and adapters, among others. Alternative preferred targets are membrane proteins, such as G protein coupled receptors (GPCRs), protein kinase receptors, transporters, and ligand-gated ion channels, among others.

Protein kinases, key signal transduction proteins that may be either membrane-associated or intracellular, catalyze the transfer of gamma phosphate from adenosine triphosphate (ATP) to a serine, threonine or tyrosine residue in a protein substrate. Radioassays, which monitor the transfer from $[\gamma\text{-}^{32}\text{P}]$ or ^{32}P -ATP, are frequently used to assay kinase activity. For instance, a scintillation assay for p56 (lck) kinase activity monitors the transfer of the gamma phosphate from $[\gamma\text{-}^{32}\text{P}]$ ATP to a biotinylated peptide substrate. The substrate is captured on a streptavidin coated bead that transmits the signal (Beveridge M *et al.*, *J Biomol Screen* (2000) 5:205-212). This assay uses the scintillation proximity assay (SPA), in which only radio-ligand bound to receptors tethered to the surface of an SPA bead are detected by the scintillant immobilized within it, allowing binding to be measured without separation of bound from free ligand. Other assays for protein kinase activity may use antibodies that specifically recognize phosphorylated substrates. For instance, the kinase receptor activation (KIRA) assay measures receptor tyrosine kinase activity by ligand stimulating the intact receptor in cultured cells, then capturing solubilized receptor with specific antibodies and quantifying phosphorylation via phosphotyrosine ELISA (Sadick MD, *Dev Biol Stand* (1999) 97:121-133). Another example of antibody based assays for protein kinase activity is TRF (time-resolved fluorometry). This method utilizes europium chelate-labeled anti-phosphotyrosine antibodies to detect phosphate transfer to a polymeric substrate coated onto microtiter plate wells. The amount of phosphorylation is then detected using time-resolved, dissociation-enhanced fluorescence (Braunwalder AF, *et al.*, *Anal Biochem* 1996 Jul 1;238(2):159-64).

Protein phosphatases catalyze the removal of a gamma phosphate from a serine, threonine or tyrosine residue in a protein substrate. Since phosphatases act in opposition

to kinases, appropriate assays measure the same parameters as kinase assays. In one example, the dephosphorylation of a fluorescently labeled peptide substrate allows trypsin cleavage of the substrate, which in turn renders the cleaved substrate significantly more fluorescent (Nishikata *M et al.*, *Biochem J* (1999) 343:35-391). In another example, fluorescence polarization (FP), a solution-based, homogeneous technique requiring no immobilization or separation of reaction components, is used to develop high throughput screening (HTS) assays for protein phosphatases. This assay uses direct binding of the phosphatase with the target, and increasing concentrations of target- phosphatase increase the rate of dephosphorylation, leading to a change in polarization (Parker GJ *et al.*, (2000) *J Biolmol Screen* 5:77-88).

Proteases are enzymes that cleave protein substrates at specific sites. Exemplary assays detect the alterations in the spectral properties of an artificial substrate that occur upon protease-mediated cleavage. In one example, synthetic caspase substrates containing four amino acid proteolysis recognition sequences, separating two different fluorescent tags are employed; fluorescence resonance energy transfer detects the proximity of these fluorophores, which indicates whether the substrate is cleaved (Mahajan NP *et al.*, *Chem Biol* (1999) 6:401-409).

Endogenous protease inhibitors may inhibit protease activity. In an example of an assay developed for either proteases or protease inhibitors, a biotinylated substrate is coated on a titer plate and hydrolyzed with the protease; the unhydrolyzed substrate is quantified by reaction with alkaline phosphatase-streptavidin complex and detection of the reaction product. The activity of protease inhibitors correlates with the activity of the alkaline phosphatase indicator enzyme (Gan Z *et al.*, *Anal Biochem* 1999) 268:151-156).

Helicases are involved in unwinding double stranded DNA and RNA. In one embodiment, an assay for DNA helicase activity detects the displacement of a radio-labeled oligonucleotide from single stranded DNA upon initiation of unwinding (Sivaraja M *et al.*, *Anal Biochem* (1998) 265:22-27). An assay for RNA helicase activity uses the scintillation proximity (SPA) assay to detect the displacement of a radio-labeled oligonucleotide from single stranded RNA (Kyono K *et al.*, *Anal Biochem* (1998) 257:120-126).

Polymerases catalyze the extension of newly synthesized DNA or RNA chains. Their activity may be monitored in an assay that uses labeled nucleotide analogs. For instance, a colorimetric polymerase assay monitors RNA synthesis using labeled ATP and GTP (Vassiliou W *et al.*, *Virology* (2000) 274:429-437).

Peptidyl-prolyl isomerase (PPIase) proteins, which include cyclophilins, FK506 binding proteins and paravulins, catalyze the isomerization of *cis-trans* proline peptide bonds in oligopeptides and are thought to be essential for protein folding during protein synthesis in the cell. Spectrophotometric assays for PPIase activity can detect isomerization of labeled peptide substrates, either by direct measurement of isomer-specific absorbance, or by coupling isomerization to isomer-specific cleavage by chymotrypsin (Schoiz C *et al.*, *FEBS Lett* (1997) 414:69-73; Janowski B *et al.*, *Anal Biochem* (1997) 252:299-307; Kullertz G *et al.*, *Clin Chem* (1998) 44:502-8). Alternative assays use the scintillation proximity or fluorescence polarization assay to screen for ligands of specific PPIases (Graziani F *et al.*, *J Biolmol Screen* (1999) 4:3-7; Dubowchik GM *et al.*, *Bioorg Med Chem Lett* (2000) 10:559-562). Assays for 3,2-trans-enoyl-CoA isomerase activity have also been described (Binstock, J. F., and Schulz, H. (1981) *Methods Enzymol.* 71:403-411; Geisbrecht BV *et al* (1999) *J Biol Chem.* 274:21797-803). These assays use 3-cis-octenoyl-CoA as a substrate, and reaction progress is monitored spectrophotometrically using a coupled assay for the isomerization of 3-cis-octenoyl-CoA to 2-trans-octenoyl-CoA.

The proteins used in the methods of this invention include enzymes involved in lipid, nucleic acid, and protein metabolism. Many different metabolic enzymes are amenable to high throughput assay development, due to well-characterized substrates and active sites, generally simple reaction mechanisms, and a general conservation in reaction mechanism. Numerous assays for metabolic enzymes (e.g., fatty acid desaturases, glycosyltransferases, mitochondrial enzymes, histone deacetylases, purine biosynthetic enzymes, etc.) have been developed.

Fatty acid desaturases catalyze the insertion of double bonds into saturated fatty acid molecules. In one application, radioassays for inhibitors of delta-5 and delta-6 fatty acid desaturase activity use thin layer chromatography to detect conversion of fatty acid substrates (Obukowicz *et al.*, *Biochem Pharmacol* (1998) 55:1045-1058).

Glycosyltransferases mediate changes in glycosylation patterns that, in turn, may affect the function of glycoproteins and/or glycolipids and, further downstream, processes of development, differentiation, transformation and cell-cell recognition. An assay for glycosyltransferase uses scintillation methods to measure the transfer of carbohydrate from radiolabeled sugar-nucleotide donor to a synthetic glycopolymer acceptor that is coupled to polyacrylamide and coated on plastic microtiter plates (Donovan RS *et al.*, *Glycoconj J* (1999) 16:607-615).

Histone deacetylation and acetylation proteins are involved in regulating chromatin structure during transcription and thus function in gene regulation. In one example, a histone deacetylase assay uses the scintillation proximity assay (SPA) and biotinylated [3H]acetyl histone H4 peptide substrate (Nare B et al., *Anal Biochem* 1999, 267:390-396).

5 Upon binding to streptavidin-coated SPA beads, the peptide substrate generates a radioactive signal, which decreases as a result of histone deacetylase activity.

The purH protein is a bifunctional enzyme that is responsible for key steps in de novo purine biosynthesis, having AICAR transformylase and IMP cyclohydrolase activities. In one application, a radioassay uses 3H-labeled intermediates and scintillation methods to measure enzyme activity (Szabados E and Christopherson RI, *Anal Biochem* 1994, 221:401-4).

Ubiquitination is a process of attaching ubiquitin to a protein prior to the selective proteolysis of that protein in the cell. Assays based on fluorescence resonance energy transfer to screen for ubiquitination inhibitors are known in the art (Boisclair MD et al., *J Biomol Screen* 2000 5:319-328).

15 DNA methylation is an epigenetic DNA modification that participates in genome stability and gene repression in vertebrates, and is involved in various stages of neoplasia. Measurements of DNA methylation may be based on immunoassays for biomarkers of methylation (Harrison XL, et al., *Chem Res Toxicol* 2001 14:295-301), or alternatively, based on fluorescence-based real-time PCR (Eads CA, et al., *Nucleic Acids Res* 2000 28:E32). Assays for DNA metabolism might include assays for DNA cleavage (Biggins JB, et al., *Proc Natl Acad Sci U S A* 2000 97:13537-42), or for polymerization (Lin K, and Ricciardi RP, *J Virol Methods* 2000 88:219-25).

RNA folds into a myriad of tertiary structures that are responsible for its diverse functions in cells. In most instances, RNA is associated with RNA-binding proteins (RBPs) that protect, stabilize, package or transport RNA, mediate RNA interactions with other biomolecules or act catalytically on RNA. The structural information obtained for RNA alone and RNA-protein complexes has elucidated a variety of RNA tertiary structures and diverse modes for RNA-protein interaction. The specific interaction of proteins with highly structured RNAs makes it possible to target unique RNA motifs with small molecules, thus making RNA an interesting target for therapeutic intervention. Assays for RNA binding or processing may be based on homogeneous scintillation proximity (Liu J, et al., *Anal Biochem* 2001 289:239-245), chemiluminescence

(Mazumder A, *Nucleic Acids Res* 1998 26:1996-2000), gel shift (Stull RA, et al., *Antisense Nucleic Acid Drug Dev* 1996 6:221-228; U.S. Pat. No. 6004749).

Adapter proteins are involved in a wide range of signaling and other cellular processes and generally facilitate protein-protein or protein-nucleic acid interactions via certain conserved motifs, including PDZ, SH2, SH3, PH, TRAF, WD40, LIM, ankyrin repeat, KH and annexin domains, etc. Assays for adapter protein activity may measure protein binding at the conserved motifs. For instance, exemplary assays for SH2 domain-containing proteins have measured binding using fluorescently labeled peptide substrate and fluorescence polarization or laser-scanning techniques (Lynch BA et al., *Anal Biochem* 1999, 275:62-73; Zuck P et al., *Proc Natl Acad Sci USA* 1999, 96: 11122-11127). An alternative SH2 binding assay uses radiolabeled peptide. An assay for protein-protein interaction at the LIM domain has used fluorescently labeled LIM-containing proteins (FHL2 and FHL3) and the fluorescence resonance energy transfer (FRET) technique (Li HY, *J Cell Biochem* 2001, 80:293-303).

15 G-protein-coupled receptors (GPCRs) comprise a large family of cell surface receptors that mediate a diverse array of biological functions. They selectively respond to a wide variety of extracellular chemical stimuli to activate specific signaling cascades. Assays may measure reporter gene activity or changes in intracellular calcium ions, or other second messengers (Durocher Y et al., *Anal Biochem* (2000) 284: 316-326; Miller TR et al., *J Biomol Screen* (1999) 4:249-258). Such assays may utilize chimeric Gα proteins that will couple to many different GPCRs and thus facilitate "universal" screening assays (Coward P et al., *Anal Biochem* (1999) 270:242-248; Milligan G and Rees S et al., *Trends Pharmacol Sci* (1999) 20:118-124).

GPCRs exert their effects through heterotrimeric G proteins, which cycle between active GTP- and inactive GDP-bound forms. Receptors catalyze the activation of G proteins by promoting exchange of GDP for GTP, while G proteins catalyze their own deactivation through their intrinsic GTPase activity. GEFs accelerate GDP dissociation and GTP binding, while GAPs stimulate GTP hydrolysis to GDP. The same assays used to monitor GPCR activity may thus be applied to monitor the activity of GEFs or GAPs. Alternatively, GEF activity may be assayed by the release of labeled GDP from the appropriate GTPase or by the uptake of labeled GTP. GAP activity may be monitored via a GTP hydrolysis assay using labeled GTP (e.g., Jones S et al., *Molec Biol Cell* (1998) 9:2819-2837).

Transporter proteins carry a range of substrates, including nutrients, ions, amino acids, and drugs, across cell membranes. Assays for modulators of transporters may use labeled substrates. For instance, exemplary high throughput screens to identify compounds that interact with different peptide and anion transporters both use fluorescently labeled substrates; the assay for peptide transport additionally uses multiscreen filtration plates (Blevitt JM et al., *J Biomol Screen* 1999, 4:87-91; Cihlar T and Ho ES, *Anal Biochem* 2000, 283:49-55).

Ion channels mediate essential physiological functions, including fluid secretion, electrolyte balance, bioenergetics, and membrane excitability. Assays for channel activity can incorporate ion-sensitive dyes or proteins or voltage-sensitive dyes or proteins, as reviewed in Gonzalez JE et al. (*Drug Discovery Today* (1999) 4:431-439). Alternative methods measure the displacement of known ligands, which may be radio-labeled or fluorescently labeled (e.g., SchMidd EL et al., *Anal Chem* (1998) 70:1331-1338).

Transcription factors control gene transcription. Electrophoretic mobility shift assay (EMSA) or gel shift assay is one of the most powerful methods for studying protein-DNA interactions. High throughput gel shift assays for transcription factors may involve fluorescence (Cyano dye Cy5) labeled oligodeoxynucleotide duplexes as specific probes and an automatic DNA sequencer for analysis (Ruscher K, et al., (2000) *J Biotechnol* 78:163-70). Alternatively high throughput methods involve colorimetric assays (Renard P, et al. (2001) *Nucleic Acids Res* 29(4):E21), or homogeneous fluorescence assays for the detection and quantification of sequence-specific DNA-binding proteins (Heyduk T, and Heyduk B (2001) *Nat Biotechnol* 20:171-6).

Nuclear receptors (NRs) are a superfamily of ligand-dependent transcription factors that mediate the effects of hormones and other endogenous ligands to regulate the expression of specific genes. High throughput assays for nuclear receptors include fluorescent polarization binding assays (Lin S, et al. (2002) *Anal Biochem* 300(1):15-21), and homogeneous time-resolved fluorescence energy transfer (Zhou G, et al. (2001) *Methods* 25:54-61), among others.

Reductases are enzymes of oxidoreductase class that catalyze reactions in which metabolites are reduced. High throughput screening assays for reductases may involve scintillation (Fernandes PB. (1998) *Curr Opin Chem Biol* 2:597-603; Delaporte E et al. (2001) *J Biomol Screen* 6:225-231).

Hydrolases catalyze the hydrolysis of a substrate such as esterases, lipases, peptidases, nucleotidases, and phosphatases, among others. Enzyme activity assays may be used to

measure hydrolase activity. The activity of the enzyme is determined in presence of excess substrate, by spectrophotometrically measuring the rate of appearance of reaction products. High throughput arrays and assays for hydrolases are known to those skilled in the art (Park CB and Clark DS (2002) *Biotech Bioeng* 78:229-235).

If an existent high-throughput assay is not available for a particular HM, its activity can be monitored using cell-based or cell-free methods. Since noncovalently associated multi-protein complexes mediate many biological processes, many effective chemical modulators will function by disrupting such complexes. If the HM belongs to a complex that is essential for protein function, appropriate assays may monitor complex formation or survival, instead of function *per se*. For instance, an appropriate cell-based assay is based on protein complementation, in which two proteins in a complex are fused to complementary fragments of the enzyme dihydrofolate reductase (DHFR). Enzyme activity of DHFR depends on proper folding of the two fragments, which in turn depends upon binding of the two complexed proteins. Two properties of DHFR can be assayed: DHFR confers viability to DHFR-negative cells in a cell survival assay, or DHFR binds a fluorescent substrate in a reporter assay (Remy I and Michnick SW, *Proc Natl Acad Sci* (1999) 96:5394-5399).

Apoptosis assays. Assays for apoptosis may be performed by terminal deoxynucleotidyl transferase-mediated digoxigenin-11-dUTP nick end labeling (TUNEL) assay. The TUNEL assay is used to measure nuclear DNA fragmentation characteristic of apoptosis (Lazebnik et al., 1994, *Nature* 371, 346), by following the incorporation of fluorescein-dUTP (Yonchara et al., 1989, *J. Exp. Med.* 169, 1747). Apoptosis may further be assayed by acridine orange staining of tissue culture cells (Lucas, R., et al., 1998, *Blood* 15:4730-41). An apoptosis assay system may comprise a cell that expresses an HM, and that optionally has defective p53 function (e.g. p53 is over-expressed or under-expressed relative to wild-type cells). A test agent can be added to the apoptosis assay system and changes in induction of apoptosis relative to controls where no test agent is added, identify candidate p53 modulating agents. In some embodiments of the invention, an apoptosis assay may be used as a secondary assay to test a candidate p53 modulating agents that is initially identified using a cell-free assay system. An apoptosis assay may also be used to test whether HM function plays a direct role in apoptosis. For example, an apoptosis assay may be performed on cells that over- or under-express HM relative to wild type cells. Differences in apoptotic response compared to wild type cells suggests that the HM plays

a direct role in the apoptotic response. Apoptosis assays are described further in US Pat. No. 6,133,437.

Cell proliferation and cell cycle assays. Cell proliferation may be assayed via

5 bromodeoxyuridine (BRDU) incorporation. This assay identifies a cell population undergoing DNA synthesis by incorporation of BRDU into newly-synthesized DNA. Newly-synthesized DNA may then be detected using an anti-BRDU antibody (Hoshino *et al.*, 1986, *Int. J. Cancer* 38, 369; Campana *et al.*, 1988, *J. Immunol. Meth.* 107, 79), or by other means.

10 Cell Proliferation may also be examined using [³H]-thymidine incorporation (Chen, J., 1996, *Oncogene* 13:1395-403; Jeoung, J., 1995, *J. Biol. Chem.* 270:18367-73). This assay allows for quantitative characterization of S-phase DNA syntheses. In this assay, cells synthesizing DNA will incorporate [³H]-thymidine into newly synthesized DNA. Incorporation can then be measured by standard techniques such as by counting of radioisotope in a scintillation counter (e.g., Beckman LS 3800 Liquid Scintillation Counter).

Cell proliferation may also be assayed by colony formation in soft agar (Sambrook *et al.*, Molecular Cloning, Cold Spring Harbor (1989)). For example, cells transformed with HM are seeded in soft agar plates, and colonies are measured and counted after two weeks incubation.

Involvement of a gene in the cell cycle may be assayed by flow cytometry (Gray JW *et al.* (1986) *Int. J. Radiat. Biol. Relat. Stud. Phys. Chem. Med.* 49:237-55). Cells transfected with an HM may be stained with propidium iodide and evaluated in a flow cytometer (available from Becton Dickinson).

25 Accordingly, a cell proliferation or cell cycle assay system may comprise a cell that expresses an HM, and that optionally has defective p53 function (e.g. p53 is over-expressed or under-expressed relative to wild-type cells). A test agent can be added to the assay system and changes in cell proliferation or cell cycle relative to controls where no test agent is added, identify candidate p53 modulating agents. In some embodiments of the invention, the cell proliferation or cell cycle assay may be used as a secondary assay to test a candidate p53 modulating agents that is initially identified using another assay system such as a cell-free assay system. A cell proliferation assay may also be used to test whether HM function plays a direct role in cell proliferation or cell cycle. For example, a cell proliferation or cell cycle assay may be performed on cells that over- or under-express

HM relative to wild type cells. Differences in proliferation or cell cycle compared to wild type cells suggests that the HM plays a direct role in cell proliferation or cell cycle.

Angiogenesis. Angiogenesis may be assayed using various human endothelial cell systems, such as umbilical vein, coronary artery, or dermal cells. Suitable assays include Alamar Blue based assays (available from Biosource International) to measure proliferation; migration assays using fluorescent molecules, such as the use of Becton Dickinson Falcon HTS FluoroBlock cell culture inserts to measure migration of cells through membranes in presence or absence of angiogenesis enhancer or suppressors; and tubule formation assays based on the formation of tubular structures by endothelial cells on Matrigel® (Becton Dickinson). Accordingly, an angiogenesis assay system may comprise a cell that expresses an HM, and that optionally has defective p53 function (e.g. p53 is over-expressed or under-expressed relative to wild-type cells). A test agent can be added to the angiogenesis assay system and changes in angiogenesis relative to controls where no test agent is added, identify candidate p53 modulating agents. In some 15 embodiments of the invention, the angiogenesis assay may be used as a secondary assay to test a candidate p53 modulating agents that is initially identified using another assay system. An angiogenesis assay may also be used to test whether HM function plays a direct role in cell proliferation. For example, an angiogenesis assay may be performed on cells that over- or under-express HM relative to wild type cells. Differences in angiogenesis compared to wild type cells suggests that the HM plays a direct role in angiogenesis.

Hypoxic Induction. The alpha subunit of the transcription factor, hypoxia inducible factor-1 (HIF-1), is upregulated in tumor cells following exposure to hypoxia in vitro. Under hypoxic conditions, HIF-1 stimulates the expression of genes known to be important in tumour cell survival, such as those encoding glycolytic enzymes and VEGF. Induction of such genes by hypoxic conditions may be assayed by growing cells transfected with HM in hypoxic conditions (such as with 0.1% O₂, 5% CO₂, and balance N₂, generated in a Napco 7001 incubator (Precision Scientific)) and normoxic conditions, followed by assessment of gene activity or expression by Taqman®. For example, a hypoxic induction assay system may comprise a cell that expresses an HM, and that optionally has a mutated p53 (e.g. p53 is over-expressed or under-expressed relative to wild-type cells). A test agent can be added to the hypoxic induction assay system and

changes in hypoxic response relative to controls where no test agent is added, identify candidate p53 modulating agents. In some embodiments of the invention, the hypoxic induction assay may be used as a secondary assay to test a candidate p53 modulating agents that is initially identified using another assay system. A hypoxic induction assay may also be used to test whether HM function plays a direct role in the hypoxic response. For example, a hypoxic induction assay may be performed on cells that over- or under-express HM relative to wild type cells. Differences in hypoxic response compared to wild type cells suggests that the HM plays a direct role in hypoxic induction.

10 **Cell adhesion.** Cell adhesion assays measure adhesion of cells to purified adhesion proteins, or adhesion of cells to each other, in presence or absence of candidate modulating agents. Cell-protein adhesion assays measure the ability of agents to modulate the adhesion of cells to purified proteins. For example, recombinant proteins are produced, diluted to 2.5g/mL in PBS, and used to coat the wells of a microtiter plate. The wells used for negative control are not coated. Coated wells are then washed, blocked with 1% BSA, and washed again. Compounds are diluted to 2x final test concentration and added to the blocked, coated wells. Cells are then added to the wells, and the unbound cells are washed off. Retained cells are labeled directly on the plate by adding a membrane-permeable fluorescent dye, such as calcein-AM, and the signal is quantified in a fluorescent microplate reader.

Cell-cell adhesion assays measure the ability of agents to modulate binding of cell adhesion proteins with their native ligands. These assays use cells that naturally or recombinantly express the adhesion protein of choice. In an exemplary assay, cells expressing the cell adhesion protein are plated in wells of a multiwell plate. Cells expressing the ligand are labeled with a membrane-permeable fluorescent dye, such as BCECF, and allowed to adhere to the monolayers in the presence of candidate agents. Unbound cells are washed off, and bound cells are detected using a fluorescence plate reader.

High-throughput cell adhesion assays have also been described. In one such assay, small molecule ligands and peptides are bound to the surface of microscope slides using a microarray spotter, intact cells are then contacted with the slides, and unbound cells are washed off. In this assay, not only the binding specificity of the peptides and modulators against cell lines are determined, but also the functional cell signaling of attached cells

using immunofluorescence techniques in situ on the microchip is measured (Falsey JR et al., Bioconj Chem. 2001 May-Jun;12(3):346-53).

Primary assays for antibody modulators

5 For antibody modulators, appropriate primary assays test is a binding assay that tests the antibody's affinity to and specificity for the HM protein. Methods for testing antibody affinity and specificity are well known in the art (Harlow and Lane, 1988, 1999, *supra*). The enzyme-linked immunosorbent assay (ELISA) is a preferred method for detecting HM-specific antibodies; others include FACS assays, radioimmunoassays, and fluorescent assays.

Primary assays for nucleic acid modulators

For nucleic acid modulators, primary assays may test the ability of the nucleic acid modulator to inhibit or enhance HM gene expression, preferably mRNA expression. In general, expression analysis comprises comparing HM expression in like populations of cells (e.g., two pools of cells that endogenously or recombinantly express HM) in the presence and absence of the nucleic acid modulator. Methods for analyzing mRNA and protein expression are well known in the art. For instance, Northern blotting, slot blotting, ribonuclease protection, quantitative RT-PCR (e.g., using the TaqMan®, PE Applied Biosystems), or microarray analysis may be used to confirm that HM mRNA expression is reduced in cells treated with the nucleic acid modulator (e.g., Current Protocols in Molecular Biology (1994) Ausubel FM *et al.*, eds., John Wiley & Sons, Inc., chapter 4; Freeman WM *et al.*, Biotechniques (1999) 26:112-125; Kallioniemi OP, Ann Med 2001, 33:142-147; Blohm DH and Guiseppe-Elie, A Curr Opin Biotechnol 2001, 12:41-47).

25 Protein expression may also be monitored. Proteins are most commonly detected with specific antibodies or antisera directed against either the HM protein or specific peptides. A variety of means including Western blotting, ELISA, or in situ detection, are available (Harlow E and Lane D, 1988 and 1999, *supra*).

Secondary Assays

Secondary assays may be used to further assess the activity of HM-modulating agent identified by any of the above methods to confirm that the modulating agent affects HM in a manner relevant to the p53 pathway. As used herein, HM-modulating agents encompass candidate clinical compounds or other agents derived from previously identified

modulating agent. Secondary assays can also be used to test the activity of a modulating agent on a particular genetic or biochemical pathway or to test the specificity of the modulating agent's interaction with HM.

Secondary assays generally compare like populations of cells or animals (e.g., two pools of cells or animals that endogenously or recombinantly express HM) in the presence and absence of the candidate modulator. In general, such assays test whether treatment of cells or animals with a candidate HM-modulating agent results in changes in the p53 pathway in comparison to untreated (or mock- or placebo-treated) cells or animals. Certain assays use "sensitized genetic backgrounds", which, as used herein, describe cells or animals engineered for altered expression of genes in the p53 or interacting pathways.

Cell-based assays

Cell based assays may use a variety of mammalian cell lines known to have defective p53 function (e.g. SAOS-2 osteoblasts, H1299 lung cancer cells, C33A and HT3 cervical cancer cells, HT-29 and DLD-1 colon cancer cells, among others, available from American Type Culture Collection (ATCC), Manassas, VA). Cell based assays may detect endogenous p53 pathway activity or may rely on recombinant expression of p53 pathway components. Any of the aforementioned assays may be used in this cell-based format. Candidate modulators are typically added to the cell media but may also be injected into cells or delivered by any other efficacious means.

Animal Assays

A variety of non-human animal models of normal or defective p53 pathway may be used to test candidate HM modulators. Models for defective p53 pathway typically use genetically modified animals that have been engineered to mis-express (e.g., over-express or lack expression in) genes involved in the p53 pathway. Assays generally require systemic delivery of the candidate modulators, such as by oral administration, injection, etc.

In a preferred embodiment, p53 pathway activity is assessed by monitoring neovascularization and angiogenesis. Animal models with defective and normal p53 are used to test the candidate modulator's effect on HM in Matrigel® assays. Matrigel® is an extract of basement membrane proteins, and is composed primarily of laminin, collagen IV, and heparin sulfate proteoglycan. It is provided as a sterile liquid at 4° C, but rapidly forms a solid gel at 37° C. Liquid Matrigel® is mixed with various angiogenic agents,

such as bFGF and VEGF, or with human tumor cells which over-express the HM. The mixture is then injected subcutaneously(SC) into female athymic nude mice (Taconic, Germantown, NY) to support an intense vascular response. Mice with Matrigel® pellets may be dosed via oral (PO), intraperitoneal (IP), or intravenous (IV) routes with the candidate modulator. Mice are euthanized 5 - 12 days post-injection, and the Matrigel® pellet is harvested for hemoglobin analysis (Sigma plasma hemoglobin kit). Hemoglobin content of the gel is found to correlate the degree of neovascularization in the gel.

In another preferred embodiment, the effect of the candidate modulator on HM is assessed via tumorigenicity assays. In one example, xenograft human tumors are implanted SC into female athymic mice, 6-7 week old, as single cell suspensions either from a pre-existing tumor or from *in vitro* culture. The tumors which express the HM endogenously are injected in the flank, 1×10^5 to 1×10^7 cells per mouse in a volume of 100 μ L using a 27 gauge needle. Mice are then ear tagged and tumors are measured twice weekly. Candidate modulator treatment is initiated on the day the mean tumor weight reaches 100 mg. Candidate modulator is delivered IV, SC, IP, or PO by bolus administration. Depending upon the pharmacokinetics of each unique candidate modulator, dosing can be performed multiple times per day. The tumor weight is assessed by measuring perpendicular diameters with a caliper and calculated by multiplying the measurements of diameters in two dimensions. At the end of the experiment, the excised tumors may be utilized for biomarker identification or further analyses. For immunohistochemistry staining, xenograft tumors are fixed in 4% paraformaldehyde, 0.1M phosphate, pH 7.2, for 6 hours at 4°C, immersed in 30% sucrose in PBS, and rapidly frozen in isopentane cooled with liquid nitrogen.

25 Diagnostic and therapeutic uses

Specific HM-modulating agents are useful in a variety of diagnostic and therapeutic applications where disease or disease prognosis is related to defects in the p53 pathway, such as angiogenic, apoptotic, or cell proliferation disorders. Accordingly, the invention also provides methods for modulating the p53 pathway in a cell, preferably a cell pre-determined to have defective p53 function, comprising the step of administering an agent to the cell that specifically modulates HM activity. Preferably, the modulating agent produces a detectable phenotypic change in the cell indicating that the p53 function is restored, i.e., for example, the cell undergoes normal proliferation or progression through the cell cycle.

The discovery that HM is implicated in p53 pathway provides for a variety of methods that can be employed for the diagnostic and prognostic evaluation of diseases and disorders involving defects in the p53 pathway and for the identification of subjects having a predisposition to such diseases and disorders.

5 Various expression analysis methods can be used to diagnose whether HM expression occurs in a particular sample, including Northern blotting, slot blotting, ribonuclease protection, quantitative RT-PCR, and microarray analysis. (e.g., Current Protocols in Molecular Biology (1994) Ausubel *et al.*, eds., John Wiley & Sons, Inc., chapter 4; Freeman *WM et al.*, Biotechniques (1999) 26:112-125; Kallioniemi *OP*, Ann Med 2001, 33:142-147; Blohm and Guiseppe-Elie, Curr Opin Biotechnol 2001, 12:41-47). Tissues having a disease or disorder implicating defective p53 signaling that express an HM, are identified as amenable to treatment with an HM modulating agent. In a preferred application, the p53 defective tissue overexpresses an HM relative to normal tissue. For example, a Northern blot analysis of mRNA from tumor and normal cell lines, or from tumor and matching normal tissue samples from the same patient, using full or partial HM cDNA sequences as probes, can determine whether particular tumors express or overexpress HM. Alternatively, the TaqMan® is used for quantitative RT-PCR analysis of HM expression in cell lines, normal tissues and tumor samples (PE Applied Biosystems).

20 Various other diagnostic methods may be performed, for example, utilizing reagents such as the HM oligonucleotides, and antibodies directed against an HM, as described above for: (1) the detection of the presence of HM gene mutations, or the detection of either over- or under-expression of HM mRNA relative to the non-disorder state; (2) the detection of either an over- or an under-abundance of HM gene product relative to the non-disorder state; and (3) the detection of perturbations or abnormalities in the signal transduction pathway mediated by HM.

Thus, in a specific embodiment, the invention is drawn to a method for diagnosing a disease in a patient, the method comprising: a) obtaining a biological sample from the patient; b) contacting the sample with a probe for HM expression; c) comparing results from step (b) with a control; and d) determining whether step (c) indicates a likelihood of disease. Preferably, the disease is cancer, most preferably a cancer as shown in TABLE 2. The probe may be either DNA or protein, including an antibody.

EXAMPLES

The following experimental section and examples are offered by way of illustration and not by way of limitation.

5 I. *Drosophila* p53 screen

The *Drosophila* p53 gene was overexpressed specifically in the wing using the vestigial margin quadrant enhancer. Increasing quantities of *Drosophila* p53 (titrated using different strength transgenic inserts in 1 or 2 copies) caused deterioration of normal wing morphology from mild to strong, with phenotypes including disruption of pattern and polarity of wing hairs, shortening and thickening of wing veins, progressive crumpling of the wing and appearance of dark "death" inclusions in wing blade. In a screen designed to identify enhancers and suppressors of *Drosophila* p53, homozygous females carrying two copies of p53 were crossed to 5663 males carrying random insertions of a piggyBac transposon (Fraser *M et al.*, Virology (1985) 145:356-361). Progeny containing insertions were compared to non-insertion-bearing sibling progeny for enhancement or suppression of the p53 phenotypes. Sequence information surrounding the piggyBac insertion site was used to identify the modifier genes. Modifiers of the wing phenotype were identified as members of the p53 pathway. Human orthologs of the modifiers are referred to herein as HM.

II. Analysis of Table 1

BLAST analysis (Altschul *et al.*, *supra*) was employed to identify Targets from *Drosophila* modifiers. The column "HM name" provides the known name abbreviations for the Targets, where available, from Genbank. "HM Acc#" and "HM Description" provide the Target protein Genbank identifier number (GI#) and description from Genbank, respectively. The length of each amino acid is in the "HM Length" column.

As discussed above, various classes of proteins are preferred targets for specific modulator types. "Target Type" column identifies each Target as a preferred target for one or more types of modulators. For example, TRIM2 (row 24) is a preferred target for antisense (AS), FBL3 (row 26) is a preferred target for both small molecule (SM) and antisense (AS), and PL6 (row 29) is a preferred target for antibody (Ab), small molecule (SM), and antisense (AS) modulators.

The "Category" column places each Target into a protein family, such as kinase, phosphatase, etc. These families were chosen based on the available literature, and

detailed protein domain and motif analysis for each Target. Various domains, signals, and functional subunits in proteins were analyzed using the PSORT (Nakai K., and Horton P., Trends Biochem Sci, 1999, 24:34-6; Kenta Nakai, Protein sorting signals and prediction of subcellular localization, Adv. Protein Chem. 54, 277-344 (2000)), PFAM (Bateman A., et al., Nucleic Acids Res, 1999, 27:260-2; <http://pfam.wustl.edu>), SMART (Ponting CP, et al., SMART: identification and annotation of domains from signaling and extracellular protein sequences. Nucleic Acids Res. 1999 Jan 1;27(1):229-32), TM-HMM (Erik L.L. Sonnhammer, Gunnar von Heijne, and Anders Krogh: A hidden Markov model for predicting transmembrane helices in protein sequences. In Proc. of Sixth Int. Conf. on Intelligent Systems for Molecular Biology, p 175-182 Ed J. Glasgow, T. Littlejohn, F. Major, R. Lathrop, D. Sankoff, and C. Sensen Menlo Park, CA: AAAI Press, 1998), and clust (Remm M, and Sonnhammer E. Classification of transmembrane protein families in the Caenorhabditis elegans genome and identification of human orthologs. Genome Res. 2000 Nov;10(11):1679-89) programs. The identified functional units for each protein are represented in the "Motif-H", "Psort-TM", and "TM-HMM" columns. The "Psort-TM", and "TM-TargetM" columns refer to predictions for possible transmembrane domains for each Target.

Protein sequences of Drosophila modifiers of p53 from screen (Example I), are represented in the "Fly Gene Acc" column by GI#, followed by the length of each Drosophila modifier protein ("Fly aa" column), their functional domains and motifs ("Motif Fly" column), and the type of interaction each modifier exhibits with the p53 pathway. The "PSCORE" column provides the BLAST score of each Target versus its Drosophila ortholog.

25 III. High-Throughput In Vitro Fluorescence Polarization Assay

Fluorescently-labeled HM peptide/substrate are added to each well of a 96-well microtiter plate, along with a test agent in a test buffer (10 mM HEPES, 10 mM NaCl, 6 mM magnesium chloride, pH 7.6). Changes in fluorescence polarization, determined by using a Fluorolite FPM-2 Fluorescence Polarization Microtiter System (Dynatech Laboratories, Inc.) relative to control values indicates the test compound is a candidate modifier of HM activity.

IV. High-Throughput In Vitro Binding Assay

³³P-labeled HM peptide is added in an assay buffer (100 mM KCl, 20 mM HEPES pH 7.6, 1 mM MgCl₂, 1% glycerol, 0.5% NP-40, 50 mM beta-mercaptoethanol, 1 mg/ml BSA, cocktail of protease inhibitors) along with a test agent to the wells of a Neutralite-avidin coated assay plate and incubated at 25°C for 1 hour. Biotinylated substrate is then added to each well and incubated for 1 hour. Reactions are stopped by washing with PBS, and counted in a scintillation counter. Test agents that cause a difference in activity relative to control without test agent are identified as candidate p53 modulating agents.

V. Immunoprecipitations and Immunoblotting

For coprecipitation of transfected proteins, 3 × 10⁶ appropriate recombinant cells containing the HM proteins are plated on 10-cm dishes and transfected on the following day with expression constructs. The total amount of DNA is kept constant in each transfection by adding empty vector. After 24 h, cells are collected, washed once with phosphate-buffered saline and lysed for 20 min on ice in 1 ml of lysis buffer containing 50 mM Hepes, pH 7.9, 250 mM NaCl, 20 mM -glycerophosphate, 1 mM sodium orthovanadate, 5 mM p-nitrophenyl phosphate, 2 mM dithiothreitol, protease inhibitors (complete, Roche Molecular Biochemicals), and 1% Nonidet P-40. Cellular debris is removed by centrifugation twice at 15,000 × g for 15 min. The cell lysate is incubated with 25 µl of M2 beads (Sigma) for 2 h at 4 °C with gentle rocking.

After extensive washing with lysis buffer, proteins bound to the beads are solubilized by boiling in SDS sample buffer, fractionated by SDS-polyacrylamide gel electrophoresis, transferred to polyvinylidene difluoride membrane and blotted with the indicated antibodies. The reactive bands are visualized with horseradish peroxidase coupled to the appropriate secondary antibodies and the enhanced chemiluminescence (ECL) Western blotting detection system (Amersham Pharmacia Biotech).

VI. Kinase assay

A purified or partially purified HM is diluted in a suitable reaction buffer, e.g., 50 mM Hepes, pH 7.5, containing magnesium chloride or manganese chloride (1-20 mM) and a peptide or polypeptide substrate, such as myelin basic protein or casein (1-10 µg/ml). The final concentration of the kinase is 1-20 nM. The enzyme reaction is conducted in microtiter plates to facilitate optimization of reaction conditions by increasing assay throughput. A 96-well microtiter plate is employed using a final volume 30-100 µl. The reaction is initiated by the addition of ³²P-gamma-ATP (0.5 µCi/ml) and incubated for 0.5

to 3 hours at room temperature. Negative controls are provided by the addition of EDTA, which chelates the divalent cation (Mg^{2+} or Mn^{2+}) required for enzymatic activity.

Following the incubation, the enzyme reaction is quenched using EDTA. Samples of the reaction are transferred to a 96-well glass fiber filter plate (MultiScreen, Millipore). The filters are subsequently washed with phosphate-buffered saline, dilute phosphoric acid (0.5%) or other suitable medium to remove excess radiolabeled ATP. Scintillation cocktail is added to the filter plate and the incorporated radioactivity is quantitated by scintillation counting (Wallace/Perkin Elmer). Activity is defined by the amount of radioactivity detected following subtraction of the negative control reaction value (EDTA quench).

VII. Expression analysis

All cell lines used in the following experiments are NCI (National Cancer Institute) lines, and are available from ATCC (American Type Culture Collection, Manassas, VA 20110-2209). Normal and tumor tissues were obtained from Impath, UC Davis, Clontech, Stratagene, and Ambion.

TaqMan analysis was used to assess expression levels of the disclosed genes in various samples.

RNA was extracted from each tissue sample using Qiagen (Valencia, CA) RNeasy kits, following manufacturer's protocols, to a final concentration of 50ng/ μ l. Single stranded cDNA was then synthesized by reverse transcribing the RNA samples using random hexamers and 500ng of total RNA per reaction, following protocol 4304965 of Applied Biosystems (Foster City, CA, <http://www.appliedbiosystems.com/>).

Primers for expression analysis using TaqMan assay (Applied Biosystems, Foster City, CA) were prepared according to the TaqMan protocols, and the following criteria: a) primer pairs were designed to span introns to eliminate genomic contamination, and b) each primer pair produced only one product.

Taqman reactions were carried out following manufacturer's protocols, in 25 μ l total volume for 96-well plates and 10 μ l total volume for 384-well plates, using 300nM primer and 250 nM probe, and approximately 25ng of cDNA. The standard curve for result analysis was prepared using a universal pool of human cDNA samples, which is a mixture of cDNAs from a wide variety of tissues so that the chance that a target will be present in appreciable amounts is good. The raw data were normalized using 18S rRNA (universally expressed in all tissues and cells).

For each expression analysis, tumor tissue samples were compared with matched normal tissues from the same patient. A gene was considered overexpressed in a tumor when the level of expression of the gene was 2 fold or higher in the tumor compared with its matched normal sample. In cases where normal tissue was not available, a universal pool of cDNA samples was used instead. In these cases, a gene was considered overexpressed in a tumor sample when the difference of expression levels between a tumor sample and the average of all normal samples from the same tissue type was greater than 2 times the standard deviation of all normal samples (i.e., Tumor - average(all normal samples) > 2 x STDEV(all normal samples)).

Results are shown in Table 2. Data presented in bold indicate that greater than 50% of tested tumor samples of the tissue type indicated in row 1 exhibited over expression of the gene listed in column 1, relative to normal samples. Underlined data indicates that between 25% to 49% of tested tumor samples exhibited over expression. A modulator identified by an assay described herein can be further validated for therapeutic effect by administration to a tumor in which the gene is overexpressed. A decrease in tumor growth confirms therapeutic utility of the modulator. Prior to treating a patient with the modulator, the likelihood that the patient will respond to treatment can be diagnosed by obtaining a tumor sample from the patient, and assaying for expression of the gene targeted by the modulator. The expression data for the gene(s) can also be used as a diagnostic marker for disease progression. The assay can be performed by expression analysis as described above, by antibody directed to the gene target, or by any other available detection method.

Table 1

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
1	Parkin1	gi 4758884 ref NP_04553.1	4553.1	4553.1	gi 4758883 ref NM_004562.1 Homo sapiens Parkinson disease (autosomal recessive, juvenile) 2, parkin (PARK2), transcript variant 1, mRNA	1	parkin isoform 1; parkin [Homo sapiens]; gi 3063338 dbj BA25751.1 Parkin [Homo sapiens]	465
2	Parkin2	gi 7669538 ref NP_054642.1	4642.1	4642.1	gi 7669537 ref NM_003987.1 Homo sapiens Parkinson disease (autosomal recessive, juvenile) 2, parkin (PARK2), transcript variant 2, mRNA	2	parkin isoform 2; parkin [Homo sapiens]	437
3	Parkin3	gi 7669540 ref NP_054643.1	4643.1	4643.1	gi 7669539 ref NM_003988.1 Homo sapiens Parkinson disease (autosomal recessive, juvenile) 2, parkin (PARK2), transcript variant 3, mRNA	3	parkin isoform 3; parkin [Homo sapiens]	316
4	P4HA1	gi 190788 gb AA36535.1	35.1	35.1	gi 190787 gb M24487.1 HUMAN PROLYL 4-HYDROXYLASE ALPHA SUBUNIT mRNA, complete cds, clone PA-15	4	prolyl 4-hydroxylase alpha subunit (EC 1.14.11.2)	534

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
5	P4HA2	gi 4758888 ref NP_04190.1	4190.1	4190.1	gi 4758887 ref NM_004199.1 Homo sapiens procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide II (P4HA2), mRNA	5	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide II; prolyl 4-hydroxylase, alpha polypeptide, type 2; prolyl-4-hydroxylase, alpha polypeptide, type II [Homo sapiens]; gi 2439985 gb AA871339.1 prolyl 4-hydroxylase	535
6	Scribble d	gi 13112035 gb AAH03193.1	3193.1	3193.1	gi 13112034 gb BC003193.1 Homo sapiens, similar to scribble, clone MGC:398, mRNA, complete cds	6	Similar to scribble [Homo sapiens]	524
7	KIAA0147	gi 146987 gb BA009768.1	768.1	768.1	gi 1469875 dbj D63487.1 D63481 Human mRNA for KIAA0147 gene, partial cds	7	The KIAA0147 gene product is related to adenylyl cyclase, [Homo sapiens]	1551
8	ERBIN	gi 8923909 ref NP_061165.1	1165.1	1165.1	gi 8923908 ref NM_008695.1 Homo sapiens erbB2-interacting protein ERBIN (LOC55914), mRNA	8	erbB2-interacting protein ERBIN [Homo sapiens]; gi 8572221 gb AA77048.1 AF283744.1 erbB2-interacting protein ERBIN [Homo sapiens]	1371

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
9	KIAA1225	gi 6330668 gb BAA866539.1	gi 6330668 gb BAA866539.1	124	gi 6330667 gb AB033051.1 AB033051 Homo sapiens mRNA for KIAA1225 protein, partial cds	9	KIAA1225 protein [Homo sapiens]	1271
10	APC10	gi 483670 gb AAD30527.1	gi 483670 gb AAD30527.1	125	gi 4836699 gb AF132794.1 AF132794 Homo sapiens anaphase promoting complex subunit 10 mRNA, complete cds	10	anaphase promoting complex subunit 10 [Homo sapiens]	185
11	KIAA1360	gi 724310 gb AB037781.1 AB037781 Homo sapiens mRNA for KIAA1360 protein, partial cds	gi 724310 gb AB037781.1 AB037781	126	gi 7243100 gb AB037781.1 AB037781 Homo sapiens mRNA for KIAA1360 protein, partial cds	11	KIAA1360 protein [Homo sapiens]	796
12	BAB14869	gi 10436614 gb BA4869.1	gi 10436614 gb BA4869.1	127	gi 10436613 gb AK024274.1 AK024274 Homo sapiens cDNA FLJ14212 fis, clone NT2RP3003500, weakly similar to SCY1 PROTEIN	12	unnamed protein product [Homo sapiens]	735
13	TRAF4	NP_004286.1	gi 4759252 ref NP_004286.1	128	gi 4759251 ref NM_004295.1	13	TNF receptor-associated factor 4 [Homo sapiens]	470
14	CAP1	AAA68195	gi 695358 gb AA68195.1	129	>gi 695357 gb L38509.1 HUMCAP1A	14	CD40-associated protein - human	543
15	TRAF2	S56163	gi 1086393 ref NP_06961.1	130	gi 10863938 ref NM_021138.1	15	tumor necrosis factor receptor-associated protein - human	501
16	TRAF3	XP_007256.1	gi 1364795 ref XP_007256.2	131	gi 13647952 ref XM_007256.3	16	TNF receptor-associated factor 3 [Homo sapiens]	640

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
17	DSCR1L1	gi 12732604 gnl NCBI GenomePr Pro TR00066904	gi 12732604 gnl NCBI GenomePr Pro TR00066904	132	gi 12732603 ref XM_004495.2 Homo sapiens Down syndrome critical region gene 1-like 1 (DSCR1L1), mRNA	17	Down syndrome critical region gene 1-like 1 protein [Homo sapiens]	197
18	DSCR1L2	gi 1730509 ref NP_038469.1	gi 1730509 ref NP_038469.1	133	gi 7305008 ref NM_03441.1 Homo sapiens Down syndrome critical region gene 1-like 2 (DSCR1L2), mRNA	18	Down syndrome critical region gene 1-like 2 protein; Down syndrome candidate region 1-like 2 [Homo sapiens]; gi 6017919 gb AF01684.1 AF176116.1 Down Syndrome candidate region 1-like protein 2 [Homo sapiens]; gi 11422951 gnl NCBI GenomePr Pro TR00066928 Down	241
19	SAP18	gi 11433775 gnl NCBI GenomePr Pro TR00069518	gi 11433775 gnl NCBI GenomePr Pro TR00069518	134	gi 13627633 ref XM_007104.2 Homo sapiens sin3-associated polypeptide, 18kD (SAP18), mRNA	19	sin3 associated polypeptide p18 [Homo sapiens]; gi 5231141 gb A041090.1 AF153608.1 sin3 associated polypeptide [Homo sapiens]; gi 2108210 gb A051322.1 sin3 associated polypeptide p18 [Homo sapiens]; gi 6831678 sp Q00422 SP18_HUMAN SIN3 ASSOCIATED POLYP	153

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
20	KIAA0957	gi 458955 gb BA023174.1	gi 458955 gb BA023174.1	135	gi 458955 gb AB023174.1	20	KIAA0957 protein [Homo sapiens]; gi 7662408 ref NP_055757.1 KIAA0957 protein [Homo sapiens]	692
21	PKB	gi 240761 gb AAC51825.1	gi 240761 gb AAC51825.1	136	gi 240761 gb AF01795 Homo sapiens 3-phosphoinositide dependent protein kinase-1 (PDK1) mRNA, complete cds	21	3-phosphoinositide dependent protein kinase-1 [Homo sapiens]; gi 2503936 emb CAA75341.1 PKB kinase [Homo sapiens]; gi 4505695 ref NP_002604.1 3-phosphoinositide dependent protein kinase-1; PKB kinase [Homo sapiens]	556

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
22	ELOVL1	gi 11427179 gnl NCBIGenomeProt TR00064446	gi 11427179 gnl NCBIGenomeProt TR00064446	137	gi 13638544 ref XM_002040.2 Homo sapiens elongation of very long chain fatty acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 1 (ELOVL1), mRNA	22	elongation of very long chain fatty acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 1 [Homo sapiens]; gi 8217571 emb CAB92758.1 dJ92O14.4 (CGI-88 protein) [Homo sapiens]; gi 12653871 gb AAH00618.1 AAH00618 elongation of very long chain fatty acids (FEN1/Elo2, S	279

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
23	ELOVL2	gi 11418666 NCBI GenomePr Pro TR00066756	gi 11418666 NCBI GenomePr Pro TR00066756	138	gi 13643290 ref XM_004347.3 Homo sapiens elongation of very long chain fatty acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 2 (ELOVL2), mRNA	23	elongation of very long chain fatty acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 2 (Homo sapiens)	324

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
24	TRIM2	gi 13446227 ref NP_056086.1	gi 13446227 ref NP_056086.1	139	gi 13446226 ref NM_015271.1 Homo sapiens tripartite motif protein TRIM2 (KIAA0517), mRNA	24	tripartite motif protein TRIM2; KIAA0517 protein (Homo sapiens); brain expressed ring finger protein [Homo sapiens]; gi 12407371 gb AA053474.1 AF220020.1 tripartite motif protein TRIM3 isoform alpha [Homo sapiens]; gi 5453589 ref NP_008449.1 ring finger protein 22; brain expressed ring finger [Homo sapiens]	744
25	ZFP270	gi 12056482 ref NP_004225.2	gi 12056482 ref NP_004225.2	140	gi 12056481 ref NM_004234.3 Homo sapiens zinc finger protein homologous to Zfp93 in mouse (ZFP93), mRNA	25	zinc finger protein 270; zinc finger protein homologous to Zfp93 in mouse (ZFP93), mRNA	738
26	FBL3	gi 5919219 gb AAD56248.1 AF188273.1	gi 5919219 gb AAD56248.1 AF188273.1	141	gi 6456734 gb AF189355.1 AF189355 Homo sapiens F-box protein FBL5 (FBL5) mRNA, complete cds	26	leucine-rich repeats containing F-box protein FBL3 [Homo sapiens]; SCF ubiquitin-protein ligase complex	423
27	KIAA1150	gi 6330051 db BAA86464.1	gi 6330051 db BAA86464.1	142	gi 6330050 db AB032976.1 AB032976 Homo sapiens mRNA for KIAA1150 protein, partial cds	27	KIAA1150 protein [Homo sapiens] - related to xenopus Mit-2 - complex couples DNA methylation to chromatin remodelling and histone deacetylation	499

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
28	ADSL2	gi 12654919 gb AAH01305.1 A AH01305	gi 12654919 gb AAH01305.1 AA H01305	143	gi 12654918 gb BC001305.1 BC001305	128	Unknown (protein for MGC:5487) [Homo sapiens]; gi 10440045 db BAB15632.1 unnamed protein product [Homo sapiens]; gi 13129088 ref NP_076995.1 hypothetical protein MGC5487 [Homo sapiens]	265

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
29	PL6	gi120902 0 gb AAA9 2281.1	gi1209020 gb AAA92 281.1	144	gi1209019 gb U09584 .; HSU09584 Human PL6 protein (PL6) mRNA, complete cds	29	PL6 protein; gi7513245 pir G 01430 PL6 protein - human; gi15902022 ref N P_008955.1 PL6 protein [Homo sapiens]; PL6 protein, unknown function but deleted in small cell lung cancer [Homo sapiens]	351

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
30	SPRY2	gi503211 5 ref NP_0 05833.1	gi5032115 ref NP_00 5833.1	145	gi5032114 ref NM_00 5842.1 Homo sapiens sprouty (Drosophila) mRNA	30	sprouty (Drosophila) homolog 2; sprouty, Drosophila, homolog of, 2 [Homo sapiens]; gi13124551 sp Q43597 SPY2_H UMAN SPROUTY HOMOLOG 2 (SPRY-2); gi2809400 gb A AC04258.1 Sprouty 2 [Homo sapiens]; gi11435347 gnl NCBIGenomePr ot TR00069819 sprouty Homolog 2 of Drosophila sprouty which is an FGF signalling antagonist Involved in determining apical branching of airways	315
31	SPRY3	gi897978 9 emb CA B96768.1	gi8979789 emb CAB 96768.1	146	gi8979788 emb AJ27 1735.1 HSA271735 Homo sapiens Xq pseudautosomal region; segment 1/2	31	sprouty (Drosophila) homolog 3 [Homo sapiens]; gi13124553 sp Q43610 SPY3_H UMAN SPROUTY HOMOLOG 3 (SPRY-3)	288

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
32	SPRY4 A	gi 12655913 gb AAK3 gb AAK00652.1 AF227516_1	gi 12655913 gb AAK3 gb AAK00652.1 AF227516_1	147	gi 12655912 gb AF227516_1 AF227516 Homo sapiens sprouty-4A mRNA, complete cds	32	sprouty-4A [Homo sapiens]	322
33	SGT1	gi 12654187 gb AAH7 gb AAH00911.1 AAH00911	gi 12654187 gb AAH7 gb AAH00911.1 AAH00911	148	gi 12654186 gb BC000911 BC000911 Homo sapiens, suppressor of G2 allele of SKP1, S. cerevisiae, homolog of, clone MGC:5348, mRNA, complete cds	33	suppressor of G2 allele of SKP1, S. cerevisiae, homolog of [Homo sapiens]; gi 5730041 ref NP_006695.1 suppressor of G2 allele of SKP1, S. cerevisiae, homolog of [Homo sapiens]; gi 4809026 gb AAD30062.1 suppressor of G2 allele of skp1 homolog SGT1 encodes an essential component of the yeast kinetochore assembly pathway and a novel subunit of the SCF ubiquitin ligase complex.	333

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
34	WDR5	gi 12642571 emb CA71 emb CA71 B88159.1	gi 12642571 emb CA71 emb CA71 B88159.1	149	gi 12642571 emb CA71 emb CA71 B88159.1 Homo sapiens mRNA for hypothetical protein (WDR5 gene), partial	34	hypothetical protein [Homo sapiens]; gi 12230771 sp Q9UGP9 WDR5_HUMAN WD-REPEAT PROTEIN 5	362
35	TBLR1	gi 12642591 gb AAK00301.1 AF314544_1	gi 12642591 gb AAK00301.1 AF314544_1	150	gi 12642591 gb AF314544_1 AF314544 Homo sapiens nuclear receptor co-repressor/HDAC3 complex subunit TBLR1 (TBLR1) mRNA, complete cds	35	nuclear receptor co-repressor/HDAC3 complex subunit TBLR1 [Homo sapiens]	514
36	BAB10	gi 10438881 gb B15310.1	gi 10438881 gb B15310.1	151	gi 10438881 gb B15310.1 Homo sapiens cDNA: FLJ22341 fls, clone HRC06032	38	(AK025994) unnamed protein product [Homo sapiens]	619

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
37	RPN1	gi 132559 sp P04843 RII1_HU MAN	gi 132559 sp P04843 RII1_HU MAN	152	gi 36052 emb Y00281.1 HSRIBIR Human mRNA for ribophorin I	37	DOLICHYL-DIPHOSPHOOLIGOSACCHARID E-PROTEIN GLYCOSYLTRANSFERASE 87 KDA SUBUNIT PRECURSOR (RIBOPHORIN I) (RPN-I); gi 88566 pir A28168 ribophorin I precursor - human; gi 4508675 ref NP_002941.1 ribophorin I (Homo sapiens); gi 36053 emb CAA68392.1 precursor; Human ribophorins I and II: the primary structure and membrane topology of two highly conserved rough endoplasmic reticulum-specific	607

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
38	KIAA1532	gi 795933 1db BAA96056.1	gi 795933 1db BAA96056.1	153	gi 795933 db AB040965.1 AB040965 Homo sapiens mRNA for KIAA1532 protein, partial cds	38	KIAA1532 protein (Homo sapiens)	601

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
39	CAC33 282	gi 13185197 emb CAC33282.1	gi 13185197 emb CA C33282.1	154	gi 13185196 emb AX083359.1 AX083359 Sequence 51 from Patent WO0112660	39	unnamed protein product [Homo sapiens]	377

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
40	Pinin	gi 4505923 ref NP_02678.1	gi 4505923 ref NP_02678.1	155	gi 4505922 ref NM_02687.1 Homo sapiens pinin, desmosome associated protein (PNN), mRNA	40	pinin, desmosome associated protein [Homo sapiens]; gi 1684847 gb AB48304.1 pinin [Homo sapiens] menA/DRS, a putative mediator of multiprotein complexes, is overexpressed in the metastasizing human melanoma cell lines ELM and MV3	743
41	IGSF4	gi 7230398 gb AAFAF42983.1 AF138903.1	gi 7230398 gb AAFAF42983.1 AF138903.1	156	gi 7767238 gb AF132811.1 AF132811 Homo sapiens nectin-like protein 2 (NECL2) mRNA, complete cds	41	immunoglobulin superfamily protein beta-like two [Homo sapiens]; gi 7767238 gb AF69025.1 AF132811.1 immunoglobulin superfamily member protein [Homo sapiens]; IGSF4 [Homo sapiens]; gi 7657228 ref NP_055148.1 immunoglobulin superfamily, member 4 [Homo sapiens]	442

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
42	NPHS1	gi 12742020 gnl NCBI GenomePr Pro TR000 ot TR0007 071761	gi 12742020 gnl NCBI GenomePr Pro TR000 ot TR0007 071761	157	gi 12742019 ref XM_009344.2 Homo sapiens nephrosis 1, congenital, Finnish type (nephin) (NPHS1), mRNA	42	nephin [Homo sapiens]; gi 3025699 gb A039887.1 nephin [Homo sapiens]; gi 10441644 gb AAG17141.1 AF190637_1 nephin [Homo sapiens]; gi 4758822 ref NP_004637.1 nephin [Homo sapiens]; gi 7513196 pir T37190 nephin - human	1241
43	SKIP43	gi 72098571 dbj BAA82341.1	gi 72098571 dbj BAA82341.1	158	gi 7209856 dbj AB036830.1 AB036830 Homo sapiens mRNA for 43-kDa form skeletal muscle and kidney enriched inositol phosphatase, complete cds	43	43-kDa form skeletal muscle and kidney enriched inositol phosphatase [Homo sapiens]	372
44	CHD1	gi 3182949 sp O14646 CHD1_H1 HUMAN	gi 3182949 sp O14646 CHD1_H1 HUMAN	159	gi 4557450 ref NM_01272.1 Homo sapiens chromodomain helicase DNA binding protein 3 (CHD3), mRNA	44	CHROMODOMAIN-HELICASE-DNA-BINDING PROTEIN 1 (CHD-1); gi 2645429 gb A087381.1 CHD1 [Homo sapiens]; gi 4557447 ref NP_001261.1 chromodomain helicase DNA binding protein 1 [Homo sapiens]	1709

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
45	FAA	gi 12739036 gnl NCBI GenomePr Pro TR000 ot TR0007 070119	gi 12739036 gnl NCBI GenomePr Pro TR000 ot TR0007 070119	160	gi 11433018 ref XM_007704.1 Homo sapiens fumarylacetoacetate (FAH), mRNA	45	fumarylacetoacetate [Homo sapiens]; fumarylacetoacetate [Homo sapiens]; gi 119778 sp P16930 FAAA_HUMAN FUMARYLACETOACETASE (FUMARYLACETOACETATE HYDROLASE) (BETA-DIKETONASE) (FAA); gi 182393 gb AA52422.1 fumarylacetoacetate hydrolase; gi 12803409 gb AAH02527.1 AAH02527 fumarylacetoacetate [Homo sapiens]; gi 106043 pir A37926 fumarylacetoacetate (EC 3.7.1.2) human	437
46	CDC14	gi 4502697 ref NP_03663.1	gi 4502697 ref NP_03663.1	161	gi 4502696 ref NM_03672.1 Homo sapiens CDC14 (cell division cycle 14, S. cerevisiae) homolog A, S. cerevisiae (CDC14A), mRNA	46	CDC14 (cell division cycle 14, S. cerevisiae) homolog A, S. cerevisiae CDC14 homolog, gene A [Homo sapiens]; gi 2662417 gb A088277.1 cdc14 homolog [Homo sapiens]	580

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
47	Cdc14B1	gi 426374 gb AAAD15415.1	gi 4263740 gb AAD15415.1	162	gi 4156157 gb AC006024 Homo sapiens PAC clone RPS-1166G19 from 7p12-p11.2, complete sequence	47	similar to Cdc14B1 phosphatase; similar to AF064104 (PID:g3136332) [Homo sapiens]	447
48	SDHD	gi 11437805 gnl NCBI BGenomePro TR00068703	gi 11437805 gnl NCBI BGenomePro TR00068703	163	gi 13636608 ref XM_006290.3 Homo sapiens hypothetical gene supported by NM_003002 (LOC82356), mRNA	48	succinate dehydrogenase complex, subunit D precursor [Homo sapiens]; gi 4506865 ref NP_002993.1 succinate dehydrogenase complex, subunit D precursor; succinate dehydrogenase ubiquinone cytochrome B small subunit [Homo sapiens]; gi 2351037 dbj BAA22034.1 cytochrome b small subunit of complex II [Homo sapiens]; gi 5295994 dbj BAA81889.1 cytochrome b of succinate dehydrogenase [Homo sapiens]; gi 3913480 sp Q14521 DHSD_H	159

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
49	MOI	gi 13449289 ref NP_085124.1	gi 13449289 ref NP_085124.1	164	gi 13449288 ref NM_030621.1 Homo sapiens helicase-mol (KIAA0926), mRNA	49	helicase-mol [Homo sapiens]; gi 5019820 dbj BAA78691.1 helicase-MOI [Homo sapiens]	1924
50	HD1	gi 2498443 sp Q13547 HDA1_HUMAN	gi 2498443 sp Q13547 HDA1_HUMAN	165	gi 13128859 ref NM_04964.2 Homo sapiens histone deacetylase 1 (HDAC1), mRNA	50	HISTONE DEACETYLASE 1 (HD1); gi 13128860 ref NP_004955.2 histone deacetylase 1; reduced polassium dependency, yeast homolog-like 1 [Homo sapiens]; gi 1277084 gb AAC50475.1 histone deacetylase HD1; gi 12653071 gb AAH00301.1 AAH00301 histone deacetylase 1 [Homo sapiens]	482
51	HD2	gi 12732423 gnl NCBI BGenomePro TR00068779	gi 12732423 gnl NCBI BGenomePro TR00068779	166	gi 13843715 ref XM_004370.3 Homo sapiens histone deacetylase 2 (HDAC2), mRNA	51	histone deacetylase 2 [Homo sapiens]	556

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
52	HD3	gi 333421 O sp O153 sp O1537 79 HDA3_9 HDA3_H HUMAN	gi 3334210 gi 3334210 gi HDA3_H HUMAN	167	gi 13128861 ref NM_03883.2 Homo sapiens histone deacetylase 3 (HDAC3), mRNA	52	HISTONE DEACETYLASE 3 (HD3) (RPD3-2); gi 12653663 gb AAH00614.1 AAH00614 histone deacetylase 3 [Homo sapiens]; gi 2661172 gb AAB88241.1 RPD3-2B [Homo sapiens]; gi 13128862 ref NP_003874.2 histone deacetylase 3 [Homo sapiens]; gi 2789656 gb AAC98927.1 histone deacetylase 3 [Homo sapiens]; gi 3201676 gb AAC26509.1 histone deacetylase 3 [Homo sapiens]	428

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
53	CSK	gi 30256 mb CAA4_2556.1	gi 30256 mb CAA4_2556.1	168	gi 30256 emb X59932.1 HSCSRCKIN Human mRNA for C-SRC-kinase	53	c-src-kinase [Homo sapiens]; gi 30315 emb CAA42713.1 put. cytoplasmic tyrosine kinase [Homo sapiens]; gi 729887 sp P41240 CSK_HUMAN TYROSINE-PROTEIN KINASE CSK (C-SRC KINASE) (PROTEIN-TYROSINE KINASE CYL); gi 88519 pir JHO559 protein-tyrosine kinase (EC 2.7.1.12) CSK - human; gi 4758078 ref NP_004374.1 c-src tyrosine kinase [Homo sapiens]; gi 6077093 emb CAB56562.1 protein tyrosine kinase [Homo sapiens]	450

Row	HM Name	HM Acc#	aa gi number	aa gi number	na gi number	na SEQ ID NO	HM Description	HM length
54	CTK	gi 1082751 p A556 25	gi 1082751 p A556 5	gi 896208 gb S75145.1 H006874S02 Homo sapiens megakaryocyte-associated tyrosine kinase (MATK) gene, exon 2	gi 896208 gb S75145.1 H006874S02 Homo sapiens megakaryocyte-associated tyrosine kinase (MATK) gene, exon 2	54	protein-tyrosine kinase (EC 2.7.1.112) matk, short splice form human; gi 13111883 gb AAH03109.1 AAH03109 megakaryocyte-associated tyrosine kinase [Homo sapiens]; gi 557272 emb C AA54493.1 HYL tyrosine kinase [Homo sapiens]; gi 12652729 gb AAH00114.1 AAH00114 megakaryocyte-associated tyrosine kinase [Homo sapiens]; gi 3702304 gb AAC62843.1 MATK_HUMAN; TYROSINE-PROTEIN KINASE CTK; PROTEIN KINASE HYL; HEMATOPOIETI	507
55	IKBKAP	gi 12002688 gb AA G43369.1 AF153419_1	gi 12002688 gb AA G43369.1 AF153419_1	gi 13133509 gb AF153419.2 AF153419 Homo sapiens Ikbap kinase complex-associated protein (IKBKAP) mRNA, complete cds	gi 13133509 gb AF153419.2 AF153419 Homo sapiens Ikbap kinase complex-associated protein (Homo sapiens)	55	Ikbap kinase complex-associated protein (Homo sapiens)	1332
56	MINT	gi 11427712 gnl NCBI BioGenomePr Proj TR00064496	gi 11427712 gnl NCBI BioGenomePr Proj TR00064496	gi 11427711 ref XM_002090.1 Homo sapiens KIAA0929 protein Mx2 interacting nuclear target (MINT) homolog (KIAA0929), mRNA	gi 11427711 ref XM_002090.1 Homo sapiens KIAA0929 protein Mx2 interacting nuclear target (MINT) homolog (Homo sapiens)	56	KIAA0929 protein Mx2 interacting nuclear target (MINT) homolog (Homo sapiens)	3371

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
57	Sno-N	gi 689231 tr TVHUSN	gi 689231 tr TVHUSN	gi 689231 tr TVHUSN	gi 4506966 ref NM_003036.1 Homo sapiens v-ski avian sarcoma viral oncogene homolog (SKI), mRNA	57	transforming protein sno-N - human; gi 4885599 ref NP_005403.1 SKI-like; SKI-RELATED ONCOGENE SNON; SnoA; SnoN [Homo sapiens]; gi 134594 ref P12757 SNON_HUMAN SKI-RELATED ONCOGENE SNON; gi 36511 emb C AA33289.1 snoN protein (AA 1 - 684) [Homo sapiens]	684

Row	HM Name	HM Acc#	aa gl number	aa SEQ ID NO	na gl number	na SEQ ID NO	HM Description	HM length
58	Cortactin	gi 299626 gb AAB26248.1	gi 299626 gb AAB26248.1	173	gi 4885204 ref NM_005231.1	58	EM51 gene product [human, Peptide, 550 aa]; gi 2489854 sp Q14247 SRC8_HUMAN SRC SUBSTRATE CORTACTIN (AMPLAXIN) (ONCOGENE EMS1); gi 182087 gb AA58455.1 amplaxin [Homo sapiens]; gi 477079 p r A48063 mammary tumor/squamous cell carcinoma-associated protein EMS1 - human; gi 4885205 ref NP_005222.1 cortactin; oncogene EMS1 [Homo sapiens]; TITLE The product of the EMS1 gene, amplified and overexpressed in	550

Row	HM Name	HM Acc#	aa gl number	aa SEQ ID NO	na gl number	na SEQ ID NO	HM Description	HM length
59	LCKBP 1	gi 123557 sp P14317 H1_HUMAN	gi 123557 sp P14317 H1_HUMAN	174	gi 32054 emb X16663.1	59	C LINEAGE CELL SPECIFIC PROTEIN- (HEMATOPOIETIC CELL- SPECIFIC LYN SUBSTRATE 1) (LCKBP1); gi 106328 p r S07633 hematopoietic lineage cell-specific protein HS1 - human; gi 32055 emb CAA34851.1 hematopoietic lineage cell protein (AA 1-488) [Homo sapiens]; gi 4885405 ref NP_005328.1 hematopoietic cell-specific Lyn substrate 1 [Homo sapiens]; [FUNCTION] SUBSTRATE OF THE ANTIGEN	488
60	ANX7	gi 128035 gb AAH02632.1 A02632	gi 1280359 gb BC002632 Homo sapiens, annexin A7, clone MGC3917, mRNA, complete cds	175	gi 12803594 gb BC002632 Homo sapiens, annexin A7, clone MGC3917, mRNA, complete cds	60	annexin A7 [Homo sapiens]; gi 113986 sp P20073 ANX7_HUMAN ANNEXIN A7 (ANNEXIN VII) (SYNEXIN); gi 338244 gb AA36616.1 synexin; gi 450211 ref NP_001147.1 annexin VII isoform 1; annexin VII (synexin); synexin [Homo sapiens]	466

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
61	ANX11	gi 8671171 emb CA594995.1	gi 8671171 emb CA594995.1	176	gi 8671170 emb AJ278463.1 HSA278463 Homo sapiens mRNA for annexin A11 (ANXA11 gene), isoform a	61	annexin A11 (Homo sapiens); gi 8671173 emb CAB94996.1 annexin A11 (Homo sapiens); gi 1082212 pir A53152 human; XI - human; gi 457317 ref NP_001148.1 annexin XI; annexin XI (56kD autoantigen) (Homo sapiens); gi 8671175 emb CAB94997.1 annexin A11 (Homo sapiens); gi 1703322 sp P50995 ANXB_HUMAN ANNEXIN A11 (ANNEXIN XI) (CALCYCLIN ASSOCIATED ANNEXIN 50) (CAP-50) (56 KDA AUTOANTIGEN)	505
62	SLC7A6a	XP_007888	gi 1364753 ref XP_007888.3	177	gi 13647529 ref XM_007888.3	62	solute carrier family 7 (cationic amino acid transporter, y+ system), member 6	515

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
63	HMT1	gi 1222986 sp Q0N622 JANM4_HUMAN 63539.1	gi 9652074 gb AAAF91390.1 AF2	178	gi 9652073 gb AF283539.1 AF263539	63	PROTEIN ARGININE N-METHYLTRANSFERASE 4; gi 9652074 gb AAAF91390.1 AF263539_1 arginine N-methyltransferase (Homo sapiens); gi 9789979 ref NP_062828.1 HMT1 (hnRNP methyltransferase, S. cerevisiae)-like 3 (Homo sapiens)	334
64	HRMT1L2	gi 7453576 gb AAAF622894.1 AF222689.2	gi 7453576 gb AAAF622894.1 AF222689.2	179	gi 7453574 gb AF222689.1 AF222689.2	64	protein arginine N-methyltransferase 1 (HRMT1L2) gene, complete cds, alternatively spliced	347

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
65	ALK6	gi 2055309 gb BA1919765.1	gi 2055309 gb BA1919765.1	180	gi 2055308 db D89675.1 D89675 Homo sapiens mRNA for bone morphogenetic protein type IB receptor, complete cds	65	bone morphogenetic protein type IB receptor [Homo sapiens]; gi 4502431 ref NP_001194.1 bone morphogenetic protein receptor, type IB; serine/threonine receptor kinase [Homo sapiens]; gi 6226778 sp O00238 BMRB_HUMAN BONE MORPHOGENE TIC PROTEIN RECEPTOR TYPE IB PRECURSOR; gi 11435743 gnl NCBI GenomePr c TF00065811 bone morphogenetic protein receptor, type IB [Homo sapiens]; gi 3377789 gb AAC28131.1	502

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
66	ALK3	gi 547778 sp P36894 gb BMRA_HUMAN	gi 547778 sp P36894 gb BMRA_HUMAN	181	gi 10882691 ref NM_020327.1 Homo sapiens activin A receptor, type IB (ACVR1B), transcript variant 2, mRNA	66	BONE MORPHOGENE TIC PROTEIN RECEPTOR TYPE IA PRECURSOR (SERINE/THREONINE-PROTEIN KINASE RECEPTOR RS) (SKR5) (ACTIVIN RECEPTOR-LIKE KINASE 3) (ALK-3); gi 402187 emb C4480257.1 ALK-3 [Homo sapiens]; gi 4757854 ref NP_004320.1 bone morphogenetic protein receptor, type IA precursor, activin A receptor, type II-like kinase 3 [Homo sapiens]; gi 2134722 p I 37163 ALK-3 -	532
67	FLJ11209	gi 127432 84 gnl NCBI GenomePr c TF00072690	gi 1274328 4 gnl NCBI GenomePr c TF00072690	182	gi 13631373 ref XM_010273.3 Homo sapiens hypothetical protein FLJ11209 (FLJ11209), mRNA	67	hypothetical protein FLJ11209 [Homo sapiens] - related to chicken 77KD muscle glycoprotein and a neurite-outgrowth-promoting protein, is important for the differentiation and the survival of the spinal motoneurons	395

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
68	dJ622L 5.2	gi 701838 emb CA B75615.1	gi 7018360 emb CAB 75615.1	183	gi 8010175 emb ALD4 8795.20 HSDJ622L5 Human DNA sequence from clone RP4-622L5 on chromosome 1p34.2-36.11. Contains the gene for Importin alpha 7 (karyopherin), up to six novel genes and the 5' end of the EIF3S2 gene for eukaryotic translation initiation factor 3 beta. Contains ESTs, STSs, >	68	dJ622L5.2 (novel protein) [Homo sapiens]	356
69	FLJ20142	gi 892314 ref NP_060156.1	gi 8923143 ref NP_060156.1	184	gi 8923142 ref NM_017686.1 Homo sapiens hypothetical protein FLJ20142 mRNA	69	hypothetical protein FLJ20142 [Homo sapiens]; gi 7020049 db JB AA90976.1 unnamed protein product [Homo sapiens]; gi 11426585 gnl NCBIGenomePr oti TR00064394 hypothetical protein FLJ20142 [Homo sapiens]	497

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
70	TXN	gi 135773 sp P10599	gi 135773 sp P10599	185	gi 4507744 ref NM_003329.1 Homo sapiens thioredoxin (TXN) mRNA	70	THIOREDOXIN (ATL-DERIVED FACTOR) (ADF) -[FUNCTION] THIOREDOXIN PARTICIPATES IN VARIOUS REDOX REACTIONS THROUGH THE REVERSIBLE OXIDATION OF ITS ACTIVE CENTER DITHIOL, TO A DISULFIDE, & CATALYZES DITHIOL-DISULFIDE EXCHANGE REACTIONS. [FUNCTION] ADF AUGMENTS THE EXPRESSION OF THE INTERLEUKIN-2	105
71	Trio	gi 864404 8 gb AAC43042.1	gi 864404 gb AAC43042.1	186	gi 8644047 gb AF091395.1 AF091395 Homo sapiens Trio isoform mRNA, complete cds	71	Trio isoform [Homo sapiens]; gi 8928460 sp O75982 TRIO_HUMAN TRIPLE FUNCTIONAL DOMAIN PROTEIN (PTPRF INTERACTING PROTEIN)	3038

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
72	Duo	gi 310819 5 gb AAC1 gb AAC15 5791.1	gi 3108195 gi 3108195 791.1	187	gi 3108194 gb U94190 .1 U94190 Homo sapientis Duo mRNA, complete cds	72	Duo [Homo sapientis]; gi 4504335 ref NP_003938.1 huntingtin-associated protein interacting protein [Homo sapientis]; gi 8928133 sp O 60229 HAPP_H UMAN HUNTINGTIN- ASSOCIATED PROTEIN- INTERACTING PROTEIN (DUO PROTEIN)	1663
73	CSTF6 4	gi 120530 11 emb C AB66681.1	gi 1205301 1 emb CA B66681.1	188	gi 12053010 emb AL1 36747.1 HSM801715 Homo sapientis mRNA; cdNA DKFZp434C1013 (from clone DKFZp434C1013); complete cds	73	cleavage stimulation factor; gi 4557493 ref NP_001316.1 cleavage stimulation factor subunit 2 [Homo sapientis]; gi 461847 sp P3 3240 CST2_HU MAN CLEAVAGE STIMULATION FACTOR, 64 KDA SUBUNIT (CSTF 64 KDA SUBUNIT) (CF-1 64 KDA SUBUNIT); gi 284047 pr A4 0220 cleavage stimulation factor 64K chain - human	616

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
74	CSTF2	NP_001316 6	gi 4557493 ref NP_001316.1	189	gi 4557492 ref NM_001325.1	74	cleavage stimulation factor subunit 2 [Homo sapientis]; Summary: CSTF2 is one of three (including CSTF1 and CSTF3) cleavage stimulation factors which combine to form CSTF which is involved in the polyadenylation and 3' end cleavage of pre- mRNAs. CSTF2 contains a ribonucleoprotein n-type RNA binding domain. CSTF2 is upregulated during activation of B cells which results in the	577

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
77	CGI-83	gi 12654127 gb AAH00878.1 A 0878.1 AAH00878	gi 12654127 gb AAH00878	192	gi 12654126 gb BC000878	77	CGI-83 protein [Homo sapiens]; gi 11359880 pir T44603 hypothetical protein CGI-83 [Imported] - human; gi 4928635 gb AAD34078.1 AF151841_1 CGI-83 protein [Homo sapiens]; gi 7705793 ref NP_057111.1 CGI-83 protein [Homo sapiens]	288
78	SAP145	gi 11739055 gb AAA97461.1	gi 11739055 gb AAA97461.1	193	gi 1173904 gb U41371	78	spliceosome associated protein; gi 249883 gb Q13435 S145_HUMAN MAN SPliceosome ASSOCIATED PROTEIN 145 (SAP 145) (SF3B150); gi 5803155 ref NP_006833.1 splicing factor 3b, subunit 2, 145kD; spliceosome associated protein 145, SF3b subunit [Homo sapiens]	872

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
75	GSTF3	gi 11437232 gnl NCBI B1GenomePro P01TR000606818	gi 11437232 gnl NCBI B1GenomePro P01TR000606818	190	gi 13639274 ref XM_008205.2 Homo sapiens cleavage stimulation factor, 3' pre-RNA, subunit 3, 77kD (CSTF3), mRNA	75	cleavage stimulation factor subunit 3 [Homo sapiens]; gi 1092656 pir J024339A cleavage stimulation factor [Homo sapiens]; gi 632498 gb AA61417.1 cleavage stimulation factor 77kDa subunit; gi 1082704 pir J50852 cleavage stimulation factor 77K chain - human; gi 4557495 ref NP_001317.1 cleavage stimulation factor subunit 3 [Homo sapiens]	717
76	NECL2	gi 7230399 gb AAAF42983.1 AF138903_1	gi 7230399 gb AAAF42983.1 AF138903_1	191	gi 7767238 gb AF132811.1 AF132811 Homo sapiens nectin-like protein 2 (NECL2) mRNA, complete cds	76	immunoglobulin superfamily protein beta-like two [Homo sapiens]; gi 7767239 gb AF69023.1 AF132811_1 immunoglobulin superfamily member protein [Homo sapiens]; IGSP4 [Homo sapiens]; gi 7657226 ref NP_055148.1 immunoglobulin superfamily, member 4 [Homo sapiens]; nectin-like protein 2	442

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
79	ZNT1	g 12382779 gb AA G53405.1	g 12382779 gb AAG53405.1	184	g 12382778 gb AF323590.1 AF323590 Homo sapiens zinc transporter 1 (ZNT1) gene, complete cds	79	zinc transporter 1 [Homo sapiens]	507

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
80	RACK1	gi 12653197 gb AAH00366.1 AH00366	gi 12653197 gb AAH00366.1 AH00366	195	gi 12653196 gb BC000368.1 BC000368	80	guanine nucleotide binding protein (G protein), beta polypeptide 2-like 1 [Homo sapiens]; gi 12652915 gb AAH00214.1 AAH00214 guanine nucleotide binding protein (G protein), beta polypeptide 2-like 1 [Homo sapiens]; gi 121027 sp P25388 GBLP_HUMAN GUANINE NUCLEOTIDE-BINDING PROTEIN BETA SUBUNIT-LIKE PROTEIN 12.3 (P205) (RECEPTOR OF ACTIVATED PROTEIN KINASE C 1) (RACK1) (GNB2-RS1); gi 106177 tbl B3	317

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
81	HLP2	gi 3023628 sp O00571 DDX3_H1 HUMAN	gi 3023628 sp O00571 DDX3_H1 HUMAN	196	gi 4503294 ref NM_001356.1 Homo sapiens DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 3 (DDX3), mRNA	181	DEAD-BOX PROTEIN 3 (HELICASE-LIKE PROTEIN 2) (HLP2) (DEAD-BOX, X ISOFORM); gi 12743305 gnl NCBI GenomePr ot TR00072697 DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 3 [Homo sapiens]; gi 4503295 ref NP_001347.1 DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 3; DEAD/H box-3 [Homo sapiens]; gi 3523150 gb A AC34298.1 DEAD box RNA helicase DDX3 [Homo sapiens]; gi 2148924 gb A AB95637.1 helicase like protein 2 [Homo sapiens]	662

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
82	HLP3	gi 6014945 sp O15523 DDXY_H1 HUMAN	gi 6014945 sp O15523 DDXY_H1 HUMAN	197	gi 4759303 ref NM_004679.1 Homo sapiens variable charge, Y chromosome (VCY), mRNA	182	DEAD-BOX PROTEIN 3, Y-CHROMOSOMA L; gi 2580556 gb A AC51832.1 dead box, Y isoform [Homo sapiens]; gi 4759126 ref NP_004651.1 DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide, Y chromosome; DEAD/H box-3, Y-linked [Homo sapiens]; gi 2580554 gb A AC51831.1 dead box, Y isoform [Homo sapiens]	660
83	RanBP16	gi 11899174 ref NP_055839.1	gi 11899174 ref NP_055839.1	198	gi 11899173 ref NM_015024.1 Homo sapiens RAN binding protein 16 (RANBP16), mRNA	83	RAN binding protein 16; KIAA0745 protein; RAN binding protein 16 [Homo sapiens]; gi 6650214 gb A AF21771.1 RAN binding protein 18 [Homo sapiens]	1087
84	RanBP17	gi 12597633 ref NP_075048.1	gi 12597633 ref NP_075048.1	199	gi 12597632 ref NM_022897.1 Homo sapiens RAN binding protein 17 (RANBP17), mRNA	84	RAN binding protein 17 [Homo sapiens]; gi 12004890 gb A AG44255.1 AF222747.1 RanBP17 [Homo sapiens]	1088

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
85	Maxi-K	gi 4504853 ref INP_002238.1	gi 4504853 ref INP_002238.1	200	gi 4504852 ref NM_002247.1 Homo sapiens potassium large conductance calcium-activated channel, subfamily M, alpha member 1 (KCNA1), mRNA	85	potassium large conductance calcium-activated channel, subfamily M, alpha member 1; Potassium large conductance calcium-activated channel, subfamily M, [Homo sapiens]; gi 606876 gb AA C50353.1 calcium activated potassium channel	1154
86	Cad23	gi 11321508 gb AA G27034.1	gi 11321508 gb AA G27034.1	201	gi 11321507 gb AY010111.1 Homo sapiens cadherin-23 (CDH23) mRNA, partial cds	86	cadherin-23 [Homo sapiens]	2552

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
87	PCGN2	gi 3242598 db BAA28023.1	gi 3242598 db BAA28023.1	202	gi 3242597 db AB015050.1 Homo sapiens mRNA for OCTN2, complete cds	87	OCTN2 [Homo sapiens]; gi 4507005 ref NP_003051.1 solute carrier family 22 (organic cation transporter), member 5 [Homo sapiens]; gi 4126718 db BAA38712.1 OCTN2 [Homo sapiens]; gi 7513217 pir JW0088 organic cation transporter protein 2 - human; gi 3273741 gb AAC24828.1 organic cation transporter OCTN2 [Homo sapiens]; gi 12731117 gnl NCBI(GenomePr o) TR00066110 solute carrier family 22 (organic cation	557
88	KIAA0750	gi 3882221 db BAA34470.1	gi 3882221 db BAA34470.1	203	gi 3882220 db AB018293.1 Homo sapiens mRNA for KIAA0750 protein, complete cds	88	KIAA0750 protein [Homo sapiens]; gi 7662284 ref NP_055447.1 KIAA0750 gene product [Homo sapiens]	1124

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
89	MAT- VIII	gi 4172971 sp Q00281 ref NP_006161.1 GIMETL_H 0420.1 UMAN	gi 4557737 ref NP_006161.1 0420.1	204	gi 4557736 ref NM_000429.1	89	S- ADENOSYLMET HIONINE SYNTHETASE ALPHA AND BETA FORMS (METHIONINE ADENOSYLTRA NSFERASE) (ADOMET SYNTHETASE) (MAT-VIII); gi 36329 emb C AA48822.1 methionine adenosyltransfer ase [Homo sapient]; gi 11429841 gnl NCBI/GenomePr ot TR00068102 methionine adenosyltransfer ase 1, alpha [Homo sapient]; gi 4557737 ref NP_000420.1 methionine adenosyltransfer ase 1, alpha [Homo sapient]; gi 479655 pir IS3	395
90	KIAA1121	gi 6329721 db BAA86 86435.1	gi 6329721 db BAA86 435.1	205	gi 14133238 db AB032947.2 Homo sapient mRNA for KIAA1121 protein, partial cds	90	KIAA1121 protein [Homo sapient]	1207

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
91	KIAA1591	gi 100472571 db B13417.1	gi 100472571 db B13417.1	206	gi 100472568 db AB046811.1 Homo sapient mRNA for KIAA1591 protein, partial cds	91	KIAA1591 protein [Homo sapient]	1018
92	purH	gi 1709935 sp P31939 PURH_HUMAN	gi 1709935 sp P31939 PURH_HUMAN	207	gi 9845513 ref NM_005978.2 Homo sapient S100 calcium-binding protein A2 (S100A2), mRNA	92	BIFUNCTIONAL PURINE BIOSYNTHESIS PROTEIN PURH [INCLUDES: PHOSPHORIBO SYLAMINOIMID AZOLECARBOX AMIDE FORMYLTRANS FERASE (AICAR TRANSFORMYL ASE); IMP CYCLOHYDROL ASE (INOSINICASE) (IMP SYNTHETASE) (ATIC)]; gi 4757802 ref NP_004035.1 S- aminoimidazole- 4-carboxamide ribonucleotide formyltransferas e/IMP cyclohydrolase; AICARFT/IMP C- HASE [Homo sapient]; gi 1263196 gb AA97405.1	591

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
93	NRM29	gi 563982 3 gb AAD4 5885.1 AF143676_1	gi 5639823 gb AAD45 885.1 AF143676_1	208	gi 5639822 gb AF143676.1 AF143676 Homo sapiens multisplicing nuclear envelope membrane protein nurim (NRM29) mRNA, partial cds	93	multisplicing nuclear envelope membrane protein nurim (Homo sapiens)	261
94	TKT	gi 172897 6 sp P29401 TKT_HUMAN	gi 1729978 sp P29401 TKT_HUMAN	209	gi 1297288 gb U55017.1 H5U55017 Human transcriptase (TKT) mRNA, complete cds	94	TRANSCRIPTOLA SE (TK); gi 1297297 gb AA98961.1 transketolase; gi 4507521 re NP_001055.1 transketolase (Homo sapiens); gi 11434224 gnl NCBI GenomePr o ITR00065516 transketolase (Homo sapiens)	823

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
95	FLJ00010	gi 104403 51 db JBAB15711.1	gi 1044035 1 db JBAB15711.1	210	gi 10440350 db AK024421.1 AK024421 Homo sapiens mRNA for FLJ00010 protein, partial cds	95	FLJ00010 protein (Homo sapiens)	772
96	prp28	gi 12803125 gb AAH02366.1 AAH02366	gi 1280312 5 gb AAH02366.1 AAH02366	211	gi 12803124 gb BC002366.1 BC002366 Homo sapiens, prp28, U5 snRNP 100 kd protein, clone MGC:8416, mRNA, complete cds	96	prp28, U5 snRNP 100 kd protein (Homo sapiens)	820
97	KIAA0801	gi 388232 3 db BAA34521.1	gi 3882323 db BAA34521.1	212	gi 3882322 db AB018344.1 AB018344 Homo sapiens mRNA for KIAA0801 protein, complete cds	97	KIAA0801 protein (Homo sapiens); gi 7662318 re NP_055644.1 KIAA0801 gene product (Homo sapiens)	1032

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
98	FLJ13159	gi 11345478 ref NP_068759.1	gi 11345478 ref NP_068759.1	213	gi 11345477 ref NM_021940.1 Homo sapiens hypothetical protein FLJ13159 (FLJ13159), mRNA	98	hypothetical protein FLJ13159 [Homo sapiens]; gi 10435055 dbj BAB14473.1 unnamed protein product [Homo sapiens]	437
99	CAB70 912.	gi 6807591 emb CA B70912.1	gi 6807591 emb CAB 70912.1	214	gi 6807590 emb AL137764.1 HS228H131 Novel human gene mapping to chromosome 1	89	hypothetical protein [Homo sapiens]	409
100	Cdc25C	gi 420023 p A3887	gi 420023 p A3887	215	gi 12408659 ref NM_001790.2 Homo sapiens cell division cycle 25C (CDC25C), transcript variant 1, mRNA	100	protein-tyrosine-phosphatase (EC 3.1.3.48); cdc25C - human; gi 180176 gb AA A35666.1 CDC25Hs ORF; gi 266561 sp P30307 MP13_HUMAN M-PHASE INDUCER PHOSPHATASE 3 (DUAL SPECIFICITY PHOSPHATASE CDC25C); gi 4502707 ref NP_001781.1 cell division cycle 25C protein, isoform a; mitosis inducer CDC25; phosphotyrosine phosphatase; m-phase inducer phosphatase 3; dual specificity phosphatase CDC25C [Homo sapiens]; gi 13169885 em	473

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
101	Cdc25B	gi 11641415 ref NP_068660.1	gi 11641415 ref NP_068660.1	216	gi 11641414 ref NM_021874.1 Homo sapiens cell division cycle 25B (CDC25B), transcript variant 4, mRNA	101	cell division cycle 25B, isoform 4; CDC25B [Homo sapiens]	601
102	Cdc25A	gi 266556 sp P30304 MP11_HUMAN	gi 266556 sp P30304 MP11_HUMAN	217	gi 4502704 ref NM_01789.1 Homo sapiens cell division cycle 25A (CDC25A), mRNA	102	M-PHASE INDUCER PHOSPHATASE 1 (DUAL SPECIFICITY PHOSPHATASE CDC25A); gi 180171 gb AA A58415.1 putative; gi 105590 p A41648 protein-tyrosine-phosphatase (EC 3.1.3.48); cdc25A - human; gi 4502705 ref NP_001780.1 cell division cycle 25A; Cdc25A; protein-tyrosine-phosphatase [Homo sapiens]	523
103	MUC2	gi 4505285 ref NP_02448.1	gi 4505285 ref NP_02448.1	218	gi 4505284 ref NM_02457.1 Homo sapiens mucin 2, intestinal/tracheal (MUC2), mRNA	103	mucin 2, intestinal/tracheal [Homo sapiens]; gi 454154 gb AA B95295.1 mucin [Homo sapiens]; gi 2506877 sp Q02817 MUC2_HUMAN MUCIN 2 PRECURSOR (INTESTINAL MUCIN 2)	5179

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
104	FBN2	gi 1345961 sp P35556 FBN2_HUMAN	gi 1345961 sp P35556 FBN2_HUMAN	219	gi 4755135 ref NM_001999.2 Homo sapiens fibrillin 2 (congenital contractural arachnodactyly) (FBN2), mRNA	104	FIBRILLIN 2 PRECURSOR; gi 437972 gb AA18950.1 fibrillin 2; gi 4503667 ref NP_001990.1 fibrillin 2 [Homo sapiens]	2911

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
105	FBN1	gi 745987 gb AA47221.1	gi 745987 gb AA47221.1	220	gi 397553 emb X63555.1 HSEFBRMR H.sapiens mRNA for fibrillin	105	fibrillin 1 precursor - human (fragment)	3002
106	SCYLP	gi 337999 gb AAA36601.1	gi 337999 gb AAA36601.1	221	gi 337998 gb M63573.1 HUMSCYLP Human secreted cyclophilin-like protein (SCYLP) mRNA, complete cds	106	secreted cyclophilin-like protein; gi 12654579 gb AAH01125.1 AAH01125 (cyclophilin B) (Homo sapiens); gi 4758950 ref NP_000833.1 peptidylprolyl isomerase B (cyclophilin B) (Homo sapiens); gi 11431876 gnl NCBI GenomePrct TR00070010 peptidylprolyl isomerase B (cyclophilin B) (Homo sapiens)	216

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
110	B3GAT 3	gi 12736805 gnl NCBI GenomePr Prof TRO0068461	gi 12736805 gnl NCBI GenomePr Prof TRO0068461	225	gi 13846223 ref XM_006048.3 Homo sapiens hypothetical gene supported by NM_012200 (LOC82089), mRNA	110	beta-1,3-glucuronidyltransferase 3 [Homo sapiens]; gi 12408654 ref NP_038332.2 beta-1,3-glucuronidyltransferase 3; glucuronosyltransferase I; Sqv-8-like protein; galactosylgalactosyltransferase in 3-beta-glucuronosyltransferase [Homo sapiens]	335
111	ManB	gi 2209015 gb JAAC51362.1	gi 2209015 gb JAAC51362.1	226	gi 2209008 gb U60894.1 HSMANBS10 Human lysosomal alpha-mannosidase (manB) gene, exon 15 and 16	11	lysosomal alpha-mannosidase [Homo sapiens]; gi 3122374 sp O00754 MA2B_H UMAN LYOSOMAL ALPHA-MANNOSIDASE PRECURSOR (MANNOSIDASE, ALPHA B) (LYOSOMAL ACID ALPHA-MANNOSIDASE) (LAMAN); gi 10834968 ref NP_000519.1 mannosidase, alpha B, lysosomal [Homo sapiens]	1010

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
112	DRG1	gi 4127988 emb CA A06775.1	gi 4127988 emb CA A06775.1	227	gi 4127987 emb AJ005940.1 HSA005940 Homo sapiens mRNA for GTP-binding protein	112	GTP-binding protein [Homo sapiens]; gi 4759796 ref NP_004138.1 developmentally regulated GTP-binding protein 1; neural precursor cell expressed, developmentally down-regulated 3 [Homo sapiens]; gi 6685390 sp Q9Y295 DRG1_H UMAN DEVELOPMENTALLY ALLY REGULATED GTP-BINDING PROTEIN 1 (DRG 1); gi 4218945 gb A012240.1 developmentally regulated GTP-binding protein [Homo sapiens]	367

Row	HM Name	HM Acc#	aa gl number	aa SEQ ID NO	na gl number	na SEQ ID NO	HM Description	HM length
113	DRG2	gi 4557537 ref NP_01379.1	gi 4557537 ref NP_01379.1	228	gi 4557536 ref NM_01388.1 Homo sapiens developmentally regulated GTP-binding protein 2 (DRG2), mRNA	113	developmentally regulated GTP-binding protein 2 [Homo sapiens]; gi 1706518 sp p55039 DRG2_HUMAN DEVELOPMENTALLY REGULATED GTP-BINDING PROTEIN 2 (DRG 2); gi 1082424 prt JA55014 GTP-binding protein DRG homolog - human; gi 577779 emb CAA56730.1 GTP-binding protein [Homo sapiens]	364

Row	HM Name	HM Acc#	aa gl number	aa SEQ ID NO	na gl number	na SEQ ID NO	HM Description	HM length
114	TPST-1	gi 3046918 gb AAC13552.1	gi 3046918 gb AAC13552.1	229	gi 3046917 gb AF038009.1 Homo sapiens tyrosylprotein sulfotransferase-1 mRNA, complete cds	114	tyrosylprotein sulfotransferase-1 [Homo sapiens]; gi 11420088 gnl NCBI Genome Project TR00037170 tyrosylprotein sulfotransferase 1 [Homo sapiens]; gi 8886059 sp Q60507 TPST_HUMAN PROTEIN-TYROSINE SULFOTRANSFERASE 1 (TYROSYLPROTEIN SULFOTRANSFERASE-1) (TPST-1); gi 4507665 ref NP_003587.1 tyrosylprotein sulfotransferase 1 [Homo sapiens]	370

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
115	TPST-2	gi 4507687 ref NP_03586.1	gi 4507667 ref NP_03586.1	230	gi 4507666 ref NM_003595.1	115	tyrosylprotein sulfotransferase 2; Tyrosylprotein phosphotransferase 2 [Homo sapiens]; gi 6686027 sp O60704 TPS2_HUMAN PROTEIN-TYROSINE SULFOTRANSFERASE 2 (TYROSYLPROTEIN SULFOTRANSFERASE-2) (TPST-2); gi 6572241 emb CAB62950.1 BK445C9.4 (tyrosylprotein sulfotransferase 2) [Homo sapiens]; gi 3108067 gb AAC34296.1 tyrosylprotein sulfotransferase-2 [Homo sapiens]; gi 12654459 gb AAH01057.1 AA	377

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
116	ABCG1	gi 8051577 ref NP_058198.1	gi 8051577 ref NP_058198.1	233	gi 8051576 ref NM_016818.1	231	ATP-binding cassette sub-family G member 1 isoform b; ATP-binding cassette member 1 (ABCG1), transcript variant 2, mRNA	662

Row	HM Name	HM Acc#	aa gi number	aa SEQ ID NO	na gi number	na SEQ ID NO	HM Description	HM length
117	WHITE 2	gi 11545924 ref NP_071452.1	gi 11545924 ref NP_071452.1	234	gi 11545923 ref NM_022169.1 Homo sapiens putative ABC transporter (WHITE2), mRNA	232	putative ABC transporter [Homo sapiens]; gi 1134254 tm b CAC17140.1 putative white family ATP-binding cassette transporter [Homo sapiens]	627

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
1	SM, AS	Ubiquitin ation	ubiquitin	TM= 0;	tmHMM=0	gi 7296395 gb AAAF51683.1 CG10523 gene product [Drosophila melanogaster] /QuerySize=467	467	ubiquitin_2 (IBH)	Cell Cycle	1.80E-128
2	SM, AS	Ubiquitin ation	ubiquitin	TM= 0;	tmHMM=0	gi 7296395 gb AAAF51683.1 CG10523 gene product [Drosophila melanogaster] /QuerySize=467	467		Cell Cycle	6.60E-112
3	SM, AS	Ubiquitin ation	ubiquitin	TM= 0;	tmHMM=0	gi 7296395 gb AAAF51683.1 CG10523 gene product [Drosophila melanogaster] /QuerySize=467	467		Cell Cycle	4.20E-102
4	SM, AS	Metabolic -aa	P4-hydroxy	TM= 0;	tmHMM=0	gi 10726381 gb AAAG22134.1 CG18749 gene product [Drosophila melanogaster] /QuerySize=454	454	2 (P4-hydroxy_al pha)		3.70E-51

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
5	SM, AS	Metabolic -aa	P4-hydroxy	TM= 0;	tmHMM =0	gi 10726381 gb AAFG22134.1 CG18749 gene product [Drosophila melanogaster] /QuerySize=454	454	2 (P4-hydroxy_apha)		4.10E-44
6	SM, AS	Adapter	14(LRR_ECDa)	TM= 0;	tmHMM =0	gi 7301474 gb AAFG56598.1 CG5462 scrib gene product [Drosophila melanogaster] /QuerySize=430	430	15 (LRR)	Apoptosis	3.40E-175
7	SM, AS	Adapter	12(LRR); 4(PDZ)	TM= 0;	tmHMM =0	gi 7301474 gb AAFG56598.1 CG5462 scrib gene product [Drosophila melanogaster] /QuerySize=430	430		Apoptosis	6.80E-151
8	SM, AS	Adapter	16(LRR); PDZ	TM= 0;	tmHMM =0	gi 7301474 gb AAFG56598.1 CG5462 scrib gene product [Drosophila melanogaster] /QuerySize=430	430		Apoptosis	1.60E-124

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
9	SM, AS	Adapter	12(LRR); PDZ	TM= 0;	tmHMM =0	gi 7301474 gb AAFG56598.1 CG5462 scrib gene product [Drosophila melanogaster] /QuerySize=430	430		Apoptosis	3.10E-95
10	SM, AS	Ubiquitination	DOM	TM= 0;	tmHMM =0	gi 7302773 gb AAFG57848.1 CG11419 gen	236	None		4.60E-71
11	SM, AS	Pkinase	STKc_zyto	TM= 0;	tmHMM =0	gi 7301728 gb AAFG56841.1 CG1951 gene product [Drosophila melanogaster] /QuerySize=834	834	pkinaase		2.70E-163
12	SM, AS	Pkinase	STKc_zyto	TM= 0;	tmHMM =0	gi 7301728 gb AAFG56841.1 CG1951 gene product [Drosophila melanogaster] /QuerySize=834	834			8.00E-144
13	SM, AS	Adapter - TRAF	RING; 4 (zif-TRAF); MATH			gi 4959432 gb AAFG34346.1 AF1197 94_1 TNF-receptor associated	486	4 (zif-TRAF); MATH		1.00E-112
14	SM, AS	Adapter - TRAF	#N/A			gi 4959432 gb AAFG34346.1 AF1197 94_1 TNF-receptor associated	486			1.00E-36
15	SM, AS	Adapter - TRAF	#N/A			gi 4959432 gb AAFG34346.1 AF1197 94_1 TNF-receptor associated	486			7.00E-34
16	SM, AS	Adapter - TRAF	#N/A			gi 4959432 gb AAFG34346.1 AF1197 94_1 TNF-receptor associated	486			1.00E-31

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact Ion	PSCORE
17	SM, AS	RNA-binding	rm	TM= 0;	tmHMM =0	g 7300117 gb AAF55285.1 CG6072 nla gene product [Drosophila melanogaster] /QuerySize=291	291	None		5.30E-45
18	SM, AS	RNA-binding	rm	TM= 0;	tmHMM =0	g 7300117 gb AAF55285.1 CG6072 nla gene product [Drosophila melanogaster] /QuerySize=291	291			8.50E-43
19	SM, AS	Transcription regulation	clust302	TM= 0;	tmHMM =0	g 7300116 gb AAF55284.1 CG6046 SAP18 gene product [Drosophila melanogaster] /QuerySize=149	149	None		5.00E-54

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact Ion	PSCORE
20	SM, AS	Adaptor	8 (ank)	TM= 0;	tmHMM =0	g 7303699 gb AAF58749.1 CG12342 gene product [Drosophila melanogaster] /QuerySize=920	920	8 (ank)		6.00E-31
21	SM, AS	Phenase	STKc_to	TM= 0;	tmHMM =0	g 7291915 gb AAF47332.1 CG1210 Pk61C gene product [alt 1] [Drosophila melanogaster] /QuerySize=538	538	STKc_to; S_TK_X_cyto	Coll Cyste	2.00E-107

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact	PSCORE
22	Ab, SM, AS	Metabolism - Lipid	(GNS1_ SUR4)	TM= 5; TM= 7; domain outside 1: 29 - 118; 45: TM TMhelix domain 20 42; 2: 61 - inside 77; TM 43 62; domain TMhelix 3: 113 - 63 85; 129; T outside M 88 107; domain TMhelix 4: 201 - 108 217; T 130; M inside domain 131 5: 231 - 136; 247; en TMhelix doplas 137 mic - 154; 28%; pl outside asma - 155 28%; v 173; acuolar TMhelix - 12%; 174 196; inside 197 202; TMhelix 203	gl/7300877[gb AAF321 56018.1 CG6921 gene product [Drosophila melanogaster] /QuerySize=321	321				6.20E-54

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact	PSCORE
23	Ab, SM, AS	Metabolism - Lipid	(GNS1_ SUR4)	TM= 1; TM= 7; domain outside 1: 262 - 1 55; 278; cyt TMhelix oplasm 56 78; lc - inside 24%; n 79 89; uclear - TMhelix 20%; v 90 112; esties outside - 12%; 113 143; TMhelix 144 163; inside 164 169; TMhelix 170 182; outside 193 206; TMhelix 207 229; inside 230 235; TMhelix	gl/7300877[gb AAF321 56018.1 CG6921 gene product [Drosophila melanogaster] /QuerySize=321	321				3.90E-48

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly Interact	PSCORE
24	AS	Transcription factor	RINGcyt BEC_Nuclear; Filamin; 6(NHL)	TM= 0;	tmHMM =0	gl 7298552 gb AAF53771.1 brat gen	1090	2 (zf-B_box); 5 NHL	2.90E-44
25	AS	Transcription factor	KRAB; 16 (zf-C2H2)	TM= 0;	tmHMM =0	gl 7298554 gb AAF53772.1 CG17568 gene product [Drosophila melanogaster] /QuerySize=501	501	7 (zf-C2H2)	9.40E-41
26	SM, AS	Ubiquitination	F-box; 5 (LRR)	TM= 0;	tmHMM =0	gl 7303582 gb AAF58635.1 CG9003 gene product [Drosophila melanogaster] /QuerySize=463	463	F-box	4.80E-166
27	SM, AS	DNA methylation	#NA	TM= 0;	tmHMM =0	gl 7294808 gb AAF50140.1 CG7983 gene product [Drosophila melanogaster] /QuerySize=915	915	None	1.40E-54

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly Interact	PSCORE
28	SM, AS	Metabolic	clust18	TM= 1; TM domain inside 1: 63 - 83; 79 cyto plasmic - outside 24%; 9 ndoplasma - smic - 66 88; 24%; n uclear - 89 136; 16%; TMhelix 137 156; outside 157 160; TMhelix 161 183; inside 184 194; TMhelix 195 217; outside 218 231; TMhelix 232	tmHMM =6; domain inside 1: 63 - 83; 79 cyto plasmic - outside 24%; 9 ndoplasma - smic - 66 88; 24%; n uclear - 89 136; 16%; TMhelix 137 156; outside 157 160; TMhelix 161 183; inside 184 194; TMhelix 195 217; outside 218 231; TMhelix 232	gl 7294075 gb AAF48430.1 Baldspot gene product [Drosophila melanogaster] /QuerySize=312	312	clust18	4.40E-79

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
29	Ab, SM, AS	Ab target - 6 TMD	IO (MPocasee)	TM= 4; TM domain inside 1: 98 - 12; 114; T M 13 35; domain outside 2: 133 - 36 97; 149; T TMhelix M 98 120; domain inside 3: 164 - 121 180; T 126; M TMhelix domain 127 4: 231 - 149; 247; en outside 150 doplas mic - 163; 36%; pl TMhelix asma - 164 20%; im 183; litocon inside 184 189; 20%; TMhelix 190 208; outside 209 222; TMhelix	tmHMM -6; domain inside 1: 98 - 12; 114; T M 13 35; domain outside 2: 133 - 36 97; 149; T TMhelix M 98 120; domain inside 3: 164 - 121 180; T 126; M TMhelix domain 127 4: 231 - 149; 247; en outside 150 doplas mic - 163; 36%; pl TMhelix asma - 164 20%; im 183; litocon inside 184 189; 20%; TMhelix 190 208; outside 209 222; TMhelix	gi7297120 gb AAF52388.1 CG9536 gene product [Drosophila melanogaster] /QuerySize=449	449			3.20E-70

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
30	AS	Intracellular signalling	#N/A	TM= 0; TM	tmHMM -0	gi13124543 sp O44783 CG1921 SPY_DROME PROTEIN SPROUTY (SPRY) /QuerySize=588	588	None		2.80E-48
31	AS	Intracellular signalling	#N/A	TM= 1; TM domain 1: 223 - 239; nu clear - 28%; cy toplas mic - 28%; m itochon drial - 20%;	tmHMM -0	gi13124543 sp O44783 CG1921 SPY_DROME PROTEIN SPROUTY (SPRY) /QuerySize=588	588			2.80E-44

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly Interact ion	PSCORE
32	AS	Intracellular signalling	#NA	TM= 1; TM domain 1: 259 - 275; cytoplasmic - 28%; nuclear - 16%; vesicles - 16%;	tmHMM =0	gi 13124543 sp O44783 CG1921 SPY_DROME PROTEIN (SPRY) /QuerySize=588	588		5.90E-41
33	SM, AS	Ubiquitination	3 (TPR)	TM= 0;	tmHMM =0	gi 7299014 gb AA154216.1 CG9617 gene product [Drosophila melanogaster] /QuerySize=177	177	None	2.20E-45

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
34	SM, AS	Adapter	7 (WD40)	TM= 0;	tmHMM =0	gi 7299015 gb AA154217.1 CG9615 gene product [Drosophila melanogaster] /QuerySize=319	319	4 (WD40)		4.90E-18
35	SM, AS	Adapter	8 (WD40)	TM= 0;	tmHMM =0	gi 7299015 gb AA154217.1 CG9615 gene product [Drosophila melanogaster] /QuerySize=319	319			1.20E-18
36	Ab, AS	Ab target - 7 TMD	clust294		tmHMM =7 tmHMM =7; gI_1043 8686_d bI_BAB 15310. 1_ TMHM M1.0 Inside 1 168 gI_1043 8686_d bI_BAB 15310. 1_ TMHM M1.0 TMhelix 187 189 gI_1043 8686_d bI_BAB 15310. 1_ TMHM M1.0 outside 180					

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
37	SM, AS	Glycosyl transferase	#N/A	TM=1; TM domain 1: 441-1439; 457;en doplas 440 mic- 459; 24%;cy inside topias 460 mic- 20%;n uclear- 16%;	tmHMM =1; domain outside 1: 441-1439; [Drosophila melanogaster] /QuerySize=1839	gl7297676[gb]AAFP52928.1 CG5364 gene product [Drosophila melanogaster] /QuerySize=1839	1839			6.10E-128

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
38	Ab, AS	Ab target -9 TMD	PA: clus284	TM=9; TM domain 1: 184-111; 200;T TMhelix M 12 34; domain outside 2: 233-35 181; 249;T TMhelix M 182 domain 204; 3: 255-Inside 271;T 205 M 230; domain TMhelix 4: 307-231 323;T 253; M outside domain 254 5: 330-257; 346;T TMhelix M 258 domain 280; 6: 358-Inside 374;T 281 M 306; domain TMhelix 7: 423-307 439;T 324; M outside domain 325 8: 460-328;	tmHMM =9; domain inside 1: 184-111; 200;T TMhelix [melanogaster] /QuerySize=416	gl7301394[gb]AAFP56521.1 CG17370 gene product [alt 2] [Drosophila melanogaster] /QuerySize=416	416 (clus294)	2	Accio alla	2.00E-23

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
39	Ab, AS	Ab target - 7 TMD	2 (clus284))	TM= 8; TM domain outside 1: 32 - 131; 48; TM TMhelix domain 32 54; 2: 80 - inside 96; TM 55 74; domain TMhelix 3: 101 - 75 97; 117; T outside M 98 106; domain TMhelix 4: 182 - 107 178; T 129; M inside domain 130 5: 208 - 209; 224; T TMhelix M 210 domain 232; 6: 261 - outside 277; T 233 M 257; domain TMhelix 7: 295 - 258 311; T 277; M inside domain 278 8: 319 - 289; 335; pla TMhelix sma - 290	gi 7301394 gb AAAF56521.1 CG17370 gene product [alt 2] [Drosophila melanogaster] /QuerySize=416	416		Apoptosis	6.00E-21	

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly Interact	PSCORE
40	AS	Cytoskeletal	(a) a serine-rich domain; (b) a glutamin e-proline, glutamin e-leucine repeat domain; and (c) an acidic domain rich in glutamic acid	TM= 0;	tmHMM =0	gi 7299238 gb AAAF54435.1 CG8383 gene product [Drosophila melanogaster] /QuerySize=302	302	None	3.20E-34
41	Ab, AS	Ab target - lg w 1TMD	(IG_ECD a)	TM= 1; TM domain outside 1: 379 - 1 373; 395; pla TMhelix sma - 374 32%; e 396; xtracell inside ular 397 442;	tmHMM =1;	gi 7299238 gb AAAF54434.1 CG12950 gene product [Drosophila melanogaster] /QuerySize=311	311	(IG_like_ECDa)	0.000002

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
42	Ab, AS	Ab target - Ig w 1TMD	{(g_ECD a); fn3	TM= 1; TM domain 1; 1063; 1059 - TMhelix 1075; 1084 xtracell ular	tmHMM =1; outside 1 1063; TMhelix 1084; inside 1087 1241;	gi 7299238 gb AAAF54434.1 CG12950 gene product [Drosophila melanogaster] /QuerySize=311	311			0.000003
43	SM, AS	Phosphatase	PPc_cy o	TM= 0;	tmHMM =0	gi 7302845 gb AAAF57919.1 CG6805 gene product [Drosophila melanogaster] /QuerySize=358	356			8.10E-52
44	SM, AS	Helicase	2 (chromo : SNF2; helicase_ C; SANT_N uclear	TM= 0;	tmHMM =0	gi 10727422 gb AAAF51527.2 CG3660 gene product [Drosophila melanogaster] /QuerySize=2702	2702		Apopto sis	6.70E-112

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
45	SM, AS	Metabolic	FAA_hyd ro	TM= 0;	tmHMM =0	gi 7292429 gb AAAF47833.1 CG14993 gene product [Drosophila melanogaster] /QuerySize=348	348	FAA_hyd rolase	Apopto sis	5.10E-150
46	SM, AS	Phosphatase	DSPc	TM= 0;	tmHMM =0	gi 7301043 gb AAAF56178.1 CG10371 gene product [Drosophila melanogaster] /QuerySize=183	183	DSPc		0.041118

Row	Target type	Category	Motif H	Pept TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
47	SM, AS	Phosphatase		TM=1; TM domain inside 1: 421-414; 437; TMhelix clear - 415 24%; v 437; asides outside 438 20%; cy 447; top las mic - 16%;	tmHMM =1; CG10371 [Drosophila melanogaster] /QuerySize=193	gl 7301043 gb AAAF193	193			0.134058
48	SM, AS	Metabolic	Hist_de acetyl	TM=1; TM domain 1: 126-142; pla sma - 32%; e xtracell ular	tmHMM =0 CG10219 [Drosophila melanogaster] /QuerySize=181	gl 7301044 gb AAAF181	181	None		4.00E-19

Row	Target type	Category	Motif H	Pept TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
49	SM, AS	Helicase	DEAD; helicase_3; C; PAZ; (Ribonuclease_3); dsrm	TM=0; tmHMM =0	gl 7302752 gb AAAF57830.1 CG6493 [Drosophila melanogaster] /QuerySize=142	57830.1 CG6493 [Drosophila melanogaster] /QuerySize=142	142	DEAD	Acetate	0.000044
50	SM, AS	Metabolic	Hist_de acetyl	TM=0; tmHMM =0	gl 7292522 gb AAAF47924.1 CG7471 Rpd3 gene product [Drosophila melanogaster] /QuerySize=520	47924.1 CG7471 Rpd3 gene product [Drosophila melanogaster] /QuerySize=520	520	Hist_de acetyl		3.40E-272
51	SM, AS	Metabolic	Hist_de acetyl	TM=0; tmHMM =0	gl 7292522 gb AAAF47924.1 CG7471 Rpd3 gene product [Drosophila melanogaster] /QuerySize=520	47924.1 CG7471 Rpd3 gene product [Drosophila melanogaster] /QuerySize=520	520			1.10E-270

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
52	SM, AS	Metabolic	N/A	TM= 0;	tmHMM =0	gi 7292522 gb AAF47824.1 CG7471 Rpd3 gene product [Drosophila melanogaster] /QuerySize=520	520			3.20E-184

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
53	SM, AS	Phinase	SH3; SH2; PTYKc_c yto	TM= 0;	tmHMM =0	gi 7299480 gb AAF54668.1 CG17309 gene product [Drosophila melanogaster] /QuerySize=819	819	SH2; PTYKc_c yto	Apopto class	8.90E-154

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly Interact	PSCORE
54	SM, AS	PKinase	SH3; SH2; PTYKc_c yb	TM= 0;	tmHMM =0	gl7299480[gb]AAF 54668.1 CG17309 gene product [Drosophila melanogaster] /QuerySize=819	819	Apoptosis	8.90E-125
55	SM, AS	Adapter	#N/A	TM= 0;	tmHMM =0	gl7299482[gb]AAF 54670.1 CG10535 gene product [Drosophila melanogaster] /QuerySize=1212	1212	NIDO_E CD	2.10E-159
56	SM, AS	RNA processing	RNA recognition motif	TM= 0;	tmHMM =0	gl10727421[gb]AA F51535.2 CG18487 spen gene product [alt 1] [Drosophila melanogaster] /QuerySize=4969	4969	Apoptosis	1.50E-99

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly Interact	PSCORE
57	SM, AS	Intracellular signalling	SK_Sno	TM= 0;	tmHMM =0	gl7290861[gb]AAF 48303.1 CG15332 gene product [Drosophila melanogaster] /QuerySize=570	570	None	0.891457

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
58	SM, AS	Adapter	7 (HS1_re p); SH3	TM= 0;	tmHMM =0	gi 7300693 gb AAF55840.1 CG3637 Cortactin gene product [Drosophila melanogaster] /QuerySize=558	558	4 (HS1_re p); SH3		1.80E-122

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
59	SM, AS	Adapter	4 (HS1_re p); SH3	TM= 1; TM domain 1: 420 - 436; nuclear - 24%; cytoplasmic - 20%; vesicles - 16%;	tmHMM =0	gi 7300693 gb AAF55840.1 CG3637 Cortactin gene product [Drosophila melanogaster] /QuerySize=558	558			1.70E-117
60	SM, AS	Adapter	4 (annexin)	TM= 0;	tmHMM =0	gi 12644162 sp P22484 CG5730 ANNEXIN IX /QuerySize=323	323	4 (annexin)		8.70E-100

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
61	SM, AS	Adapter	4 (annexin)	TM= 0;	tmHMM =0	gl12644162[sp1P2 2464] CG5730 ANX9_DROME ANNEXIN IX /QuerySize=323	323			1.70E-99
62	Ab, SM, AS	transport er - aa	clust118			gl17302046[gbIAAF 57148.1] CG1807 gene product [Drosophila melanogaster]	518		Apoptosis	9.50E-161

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
63	SM, AS	Metabolic -aa	#N/A	TM= 0;	tmHMM =0	gl17299276[gbIAAF 54471.1] CG5358 gene product [Drosophila melanogaster] /QuerySize=529	529	None		1.20E-59
64	SM, AS	Metabolic -aa	#N/A	TM= 0;	tmHMM =0	gl17299276[gbIAAF 54471.1] CG5358 gene product [Drosophila melanogaster] /QuerySize=529	529			2.90E-58

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
65	Ab, SM, AS	Pkinase	Activin_L ecp; GS_cyto; pkinase	TM= 1; TM domain outside 1: 128 - 1 125; clear - 126 28%; cy 148; topolmic - 149 24%; m 502; ltochon drial - 24%;	tmHMM =1; domain outside 1: 128 - 1 125; TMhelix [Drosophila melanogaster] /QuerySize=545	gi 7286958 gb AAAF54552230.1 CG14028 tkv gene product [Drosophila melanogaster] /QuerySize=545	545	Activin_L ecp; pkinase		1.90E-160

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
66	Ab, SM, AS	Pkinase	Activin_L ecp; pkinase	TM= 1; TM domain outside 1: 154 - 1 152; 170; cy 175; oplasm 153 ic - 175; 28%; n inside uclear - 176 24%; m 532; ltochon drial - 24%;	tmHMM =1; domain outside 1: 154 - 1 152; TMhelix [Drosophila melanogaster] /QuerySize=545	gi 7286958 gb AAAF54552230.1 CG14028 tkv gene product [Drosophila melanogaster] /QuerySize=545	545			1.40E-156
67	Ab, AS	Ab target - secreted	#N/A	TM= 0;	tmHMM =0	gi 7301391 gb AAAF565518.1 CG5886 gene product [Drosophila melanogaster] /QuerySize=514	514	None		9.70E-70

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
68	Ab, AS	Ab target - secreted	#N/A	TM= 0;	tmHMM =0	gl 7301391 gb AAF51456518.1 CG5886 gene product [Drosophila melanogaster] /QuerySize=514	514			2.50E-69
69	Ab, AS	Ab target - secreted	1A1pp_Nuclear; EC14_cy to	TM= 0;	tmHMM =0	gl 10727766 gb AA G22306.1 CG18813 gene product [alt 2] [Drosophila melanogaster] /QuerySize=243	243	SEC14_cyto		1.80E-64

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
70	SM, AS	Metabolic/thored					106			2.00E-29
71	SM, AS	G protein - GEF	SEC14_cyto; 7 (spectrin); 2 (RhoGEF); 2 (PH); 2 (SH3); 2 (lg); STKc_cyto	TM= 0;	tmHMM =0	gl 10727213 gb AA F47436.2 CG9208 ttrio gene product [Drosophila melanogaster] /QuerySize=1872	1872	SEC14_cyto; 7 (spectrin); RhoGEF; PH		0.00E+00

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
72	SM, AS	G protein - GEF	SEC14_cyto: 9 (spectrin); RhoGEF: PH	TM= 0;	tmHMM =0	gl110727213gbAA1872 F47436.2 CG9208 tto gene product [Drosophila melanogaster] /QuerySize=1872	1872			4.90E-287
73	SM, AS	RNA processing		TM= 0;	tmHMM =0	gl17300420gbAAAF398 55577.1 CG7697 CstF-64 gene product [Drosophila melanogaster] /QuerySize=398	398	rrm		7.60E-87

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
74	SM, AS	RNA processing	RRM							

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
75	SM, AS	RNA processing	10 (HAT_ot her)	TM=0;	tmHMM =0	gi 135031 sp P25991 CG17170 SUF_DROME SUPPRESSOR OF FORKED PROTEIN /QuerySize=732	732	10 (HAT_Ot her)		2.50E-159
76	Ab, SM, AS	Ab target 3 -lg w- 1TMD	(IG_like -ECDa); 4.1m_c yto	TM= 1;TM domain outside 1: 379-1.373; 395;pla sma - 374 32%;e 396; xtracell ular 397 442;	tmHMM =1;	gi 7299772 gb AAAF54952.1 CG14372 gene product [Drosophila melanogaster] /QuerySize=349	349			0.000041

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
77	SM, AS	Glycosyl transferase	lactama se_B	TM=0;	tmHMM =0	gi 7297345 gb AAAF52605.1 CG12375 gene product [Drosophila melanogaster] /QuerySize=291	291			2.30E-80
78	SM, AS	RNA processing	SAP; processin MAM33; SAP	TM=0;	tmHMM =0	gi 7295859 gb AAAF51159.1 CG3605 gene product [Drosophila melanogaster] /QuerySize=733	733			3.00E-245

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
79	Ab, SM, AS	transporter	3 (Cation _efflux)	TM= 6; TM domain inside 1: 12 - 6; 28; TM TMhelix domain 7 29; 2: 41 - outside 57; TM 30 43; domain TMhelix 3: 82 - 44 61; 98; TM inside domain 62 80; 4: 114 - TMhelix 130; T 81 98; M outside domain 99 112; 5: 248 - TMhelix 264; T 113 M 135; domain inside 6: 313 - 136 328; en 248; doplas TMhelix mic - 249 36%; pl 271; asma - outside 20%; m 272 ltochon 313; drial - TMhelix 20%; 314 336; Inside	gl 7296322 gb AAF51612.1 CG5130 gene product [Drosophila melanogaster] /QuerySize=512	512	Cation _efflux		1.70E-24	

Row	Target type	Category	Motif H	Port TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
80	SM, AS	Adapter	7 (WD40)	TM= 0;	tmHMM =0	gl 7297305 gb AAF52566.1 CG7111 Rack1 gene product [Drosophila melanogaster] /QuerySize=317	317	7 (WD40)	Apoptosis	2.90E-177

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact Ion	PSCORE
81	SM, AS	Helicase	DEAD; helicase _C	TM= 0;	tmHMM =0	gi 7299061 gb AAF54262.1 CG9748 gene product [Drosophila melanogaster] /QuerySize=797	797	2 (DEAD); helicase _C		8.10E-232

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact Ion	PSCORE
82	SM, AS	Helicase	DEAD; helicase _C	TM= 0;	tmHMM =0	gi 7299061 gb AAF54262.1 CG9748 gene product [Drosophila melanogaster] /QuerySize=797	797			1.40E-226
83	SM, AS	Nuclear transport	#N/A	TM= 0;	tmHMM =0	gi 7293158 gb AAF48542.1 CG9126 gene product [Drosophila melanogaster] /QuerySize=1065	1065			4.60E-171
84	SM, AS	Nuclear transport	#N/A	TM= 0;	tmHMM =0	gi 7293158 gb AAF48542.1 CG9126 gene product [Drosophila melanogaster] /QuerySize=1065	1065			2.80E-158

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly interaction	PSCORE
85	Ab, SM, AS	Channel	clust9	TM= 8; TM domain outside 1: 67 - 161; 83; TM domain 62 84; 2: 155 - inside 171; T 85 154; M TMhelix domain 155 3: 195 - 174; 211; T outside M 175 domain 188; 4: 224 - TMhelix 240; T 189 M 211; domain inside 5: 276 - 212 292; T 275; M TMhelix domain 276 6: 344 - 298; 360; T outside M 289 domain 312; 7: 593 - TMhelix 609; T 313 M 332; domain inside 8: 759 - 333 775; pla 338;	gi 7301192 gb AAAF59324.1 CG10693 sio gene product [Drosophila melanogaster] /QuerySize=1174	1174		0	
86	Ab, SM, AS	Ab target - Cadherin w 1TMD	clust19 (cadherin)	TM= 1; TM domain outside 1: 1 2265; 2267 - TMhelix 2283; c 2266 ytopias 2288; mic - inside 24%; n 2289 nuclear - 2552; 20%; v esicles - 16%;	TM= 1; TM domain outside 1: 1 2265; 2267 - TMhelix 2283; c 2266 ytopias 2288; mic - inside 24%; n 2289 nuclear - 2552; 20%; v esicles - 16%;	gi 10727403 gb AAAF51468.2 CG17941 ds gene product [Drosophila melanogaster] /QuerySize=3502	3502		9.20E-210

Row	Target type	Category	Motif H	Port TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
87	Ab, SM, AS	transporter - cation	clust105	TM= 10; TM domain 1: 20 - 20; 36; TM TMhelix domain 21 43; 2: 144 - outside 160; T 44 141; M TMhelix domain 142 3: 193 - 164; 209; T inside M 165 domain 170; 4: 233 - TMhelix 249; T 171 M 190; domain outside 5: 258 - 191 274; T 194; M TMhelix domain 195 6: 340 - 217; 356; T inside M 218 domain 228; 7: 378 - TMhelix 394; T 229 M 251; domain outside 8: 404 - 252 420; T 255;	tmHMM =12; domain inside 1 gene product [Drosophila melanogaster] /QuerySize=418	418	clust105		5.60E-49	
88	SM, AS	Adapter	CH; LIM	TM= 0; TM= 0;	tmHMM =0	gi 7299283 gb AAAF54478.1 CG11685 gene product [alt 1] [Drosophila melanogaster] /QuerySize=1194	1194	pyr_redo x; LIM		3.10E-214

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
89	SM, AS	Metabolic -aa		TM= 0;	tmHMM =0	g 17296263 gb AAF51554.1 CG2874 M(2)21AB gene product [alt 2] [Drosophila melanogaster]	427			6.80E-205
90	SM, AS	Adapter	PH	TM= 1; TM domain 1: 1031 - 1047; cytoplasmic - 20%; nuclear - 20%; vesicles - 16%;	tmHMM =0	g 10729714 gb AAF45454.2 CG18026 Caps gene product [Drosophila melanogaster] /QuerySize=1518	1518	PH		0

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
91	SM, AS	Adapter	PH	TM= 1; TM domain 1: 844 - 860; cytoplasmic - 20%; nuclear - 16%; vesicles - 16%;	tmHMM =0	g 10729714 gb AAF45454.2 CG18026 Caps gene product [Drosophila melanogaster] /QuerySize=1518	1518			0
92	SM, AS	Metabolic -aa	#N/A	TM= 0;	tmHMM =0	g 7301227 gb AAF58358.1 CG11089 gene product [Drosophila melanogaster] /QuerySize=589	589	MGS: AICARF T_IMPC Has		5.90E-290

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly Interact ion	PSCORE
93	SM, AS	Nuclear transport	transket olase	TM= 4; TM domain 1: 58 - 4; 74; TM domain 5 27; 2: 141 - outside 157; T M TMhelix domain 58 80; 3: 198 - inside 214; T M TMhelix domain 93 115; 4: 217 - outside 233; en 116 doplas 134; mic - TMhelix 32%; pl 135 asma - 157; 24%; m inside ltochon 158 drial - 261; 24%;	tmHMM =4; inside 1 TMhelix melanogaster] /QuerySize=252	gj7300293[gb AAAF252 55455.1 CG7855 gene product [Drosophila melanogaster] /QuerySize=252	252		1.80E-29
94	SM, AS	Metabolic		TM= 0;	tmHMM =0	gj7290065[gb AAAF625 54265.1 CG8036 gene product [Drosophila melanogaster] /QuerySize=625	625	2 (transket olase)	6.30E-257

Row	Target type	Category	Motif H	Sort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly Interact ion	PSCORE
95	Ab, SM, AS	transport er - cation		TM= 10; TM domain 1: 26 - 23; 42; TM domain 24 46; 2: 56 - outside 72; TM 47 49; domain TMhelix 3: 125 - 50 72; 141; T inside M 73 120; domain TMhelix 4: 161 - 121 177; T 143; M outside domain 144 5: 197 - 155; 213; T TMhelix M 156 domain 178; 8: 254 - inside 270; T 179 M 190; domain TMhelix 7: 274 - 191 290; T 213; M outside domain 214 8: 316 - 274; 332; T TMhelix M 275	tmHMM =7; inside 1 gene product [Drosophila melanogaster] /QuerySize=940	gj7298458[gb AAAF940 53678.1 CG10413 gene product [Drosophila melanogaster] /QuerySize=940	940		1.20E-188
96	SM, AS	Helicase	helicase _C	TM= 0;	tmHMM =0	gj7298459[gb AAAF801 53680.1 CG10333 gene product [Drosophila melanogaster] /QuerySize=801	801	DEAD; helicase_ C; plant_thl online	0
97	SM, AS	Helicase	2 DEAD, h ellicase_ C	TM= 0;	tmHMM =0	gj7298459[gb AAAF801 53680.1 CG10333 gene product [Drosophila melanogaster] /QuerySize=801	801		8.80E-101

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
98	SM, AS	G protein - GAP	ArfGap	TM= 0;	tmHMM =0	gjl7303978 gb AAF59021.1 CG8243 gene product [Drosophila melanogaster] /QuerySize=517	517	ArfGap		1.40E-57
99	SM, AS	G protein - GAP	ArfGap	TM= 0;	tmHMM =0	gjl7303978 gb AAF59021.1 CG8243 gene product [Drosophila melanogaster] /QuerySize=517	517			1.60E-51
100	SM, AS	Phosphatase	Rhodanase	TM= 0;	tmHMM =0	gjl12644155 sp P20483 CG1395 M-PIIP_DROME M-PHASE INDUCER PHOSPHATASE (STRING PROTEIN) (CDC25-LIKE PROTEIN) /QuerySize=478	478	Rhodanase		2.20E-56

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
101	SM, AS	Phosphatase	Rhodanase	TM= 0;	tmHMM =0	gjl12644155 sp P20483 CG1395 M-PIIP_DROME M-PHASE INDUCER PHOSPHATASE (STRING PROTEIN) (CDC25-LIKE PROTEIN) /QuerySize=478	478			2.20E-56
102	SM, AS	Phosphatase	Rhodanase	TM= 0;	tmHMM =0	gjl12644155 sp P20483 CG1395 M-PIIP_DROME M-PHASE INDUCER PHOSPHATASE (STRING PROTEIN) (CDC25-LIKE PROTEIN) /QuerySize=478	478			6.80E-54
103	Ab, SM, AS	Ab target - secreted	0	TM= 0;	tmHMM =0	gjl7296302 gb AAF51592.1 CG5847 gene product [Drosophila melanogaster] /QuerySize=2283	2283			7.60E-101

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
104	Ab, SM, AS	Ab target - EGF repeat ECM protein	3 EGF.E GF,TB, 2 EGF.E GF,TB, 5 EGF.E GF,TB, 3 EGF.E GF,TB, EGF,TB ,12 EGF.E GF,TB, 2 EGF.E GF,TB, 7 EGF.E GF,TB, 5 EGF.E GF,TB, 7 EGF.ca dherin	TM= 0; =1; inside 1 8; TMhelix 7 26; outside 27 2911;	gl 7295695 gb AAAF51000.1 CG15637 gene product [Drosophila melanogaster] /QuerySize=3679	3679 (EGF)			2.10E-128	

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact Ion	PSCORE
105	Ab, SM, AS	Ab target - EGF repeat ECM protein	3 EGF,E GF,TB, 2 EGF,E GF,TB, 5 EGF,E GF,TB, 3 EGF,E GF,TB, EGF,TB ,12 EGF,E GF,TB, 2 EGF,E GF,TB, 7 EGF,E GF,TB, 5 EGF,E GF,TB	TM= 0; TM=1; Inside 1 10; TMhelix 11 33; outside 34 216;	tmHMM =0	gi 7295685 gb AAAF51000.1 CG15637 gene product [Drosophila melanogaster] /QuerySize=3679	3679			3.50E-128
106	Ab, SM, AS	isomerase	pro Iso merase	TM= 0; TM=1; Inside 1 10; TMhelix 11 33; outside 34 216;	tmHMM =1; Inside 1 10; TMhelix 11 33; outside 34 216;	gi 7291447 gb AAAF46873.1 CG2852 gene product [alt 1][Drosophila melanogaster] /QuerySize=204	204	pro Iso merase		6.90E-91

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
107	Ab, SM, AS	isomerase	protease	TM=0;	tmHMM=1; Inside 1 6; TMhelix 7 28; outside 30 212;	gl 7291447 gb AAAF46873.1 CG28521 Drosophila melanogaster gene product [alt 1] /QuerySize=204	204			2.20E-60

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
108	SM, AS	Glycosyltransferase	#N/A	TM=0;	tmHMM=0	gl 7291489 gb AAAF46924.1 CG34951 Drosophila melanogaster gene product /QuerySize=320	320			3.60E-130
109	SM, AS	Glycosyltransferase	#N/A	TM=0;	tmHMM=1; Inside 1 6; TMhelix 7 24; outside 25 334;	gl 7297540 gb AAAF52795.1 CG38811 Drosophila melanogaster gene product /QuerySize=442	442	None		4.30E-49

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
110	SM, AS	Glycosyl transferase	Glyco_hydro_38	TM=1; domain inside 1: 8-6; 24; TM helix domain 7 29; 2: 121 - outside 137; T 30 335; M domain 3: 248 - 264; en doplas mic - 32%; m itochon drial - 28%; pl asma - 16%;	tmHMM=1; domain inside 1: 8-6; 24; TM helix domain 7 29; 2: 121 - outside 137; T 30 335; M domain 3: 248 - 264; en doplas mic - 32%; m itochon drial - 28%; pl asma - 16%;	gi 7297540 gb AAAF52795.1 CG3881 gene product [Drosophila melanogaster] /QuerySize=442	442			8.10E-49
111	SM, AS	Glycosyl transferase			tmHMM=0	gi 7297706 gb AAAF52958.1 CG6206 gene product [Drosophila melanogaster] /QuerySize=1071	1071	Glyco_hydro_38		2.00E-268

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
112	SM, AS	G protein - GTP-binding	GTP1_OBG	TM=1; TM domain 1: 30 - 46; mito chondrial - 40%; cyto plas mic - 16%; e ndoplas mic - 12%;	tmHMM=0	gi 7303536 gb AAAF58591.1 CG6340 128up gene product [Drosophila melanogaster] /QuerySize=367	367	GTP1_OBG		2.40E-210

Row	Target type	Category	Motif H	Peort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
113	SM, AS	G protein - GTP- binding	GTP1 - OBG	TM= 1; TM domain 1: 135 - 151; cytoplasmic - 24%; a ndoplas mic - 20%; n uclear - 20%;	TM= 1; TM domain 1: 9 - 25; end oplasm ic - 28%; cy toplas mic - 20%; n uclear - 20%; - Golgi	[Drosophila melanogaster] CG8340 product [QuerySize=367]	[Drosophila melanogaster] CG8340 product [QuerySize=367]			6.50E-140

Row	Target type	Category	Motif H	Peort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
114	SM, AS	Glycosyl transferase	#N/A	TM= 1; TM domain 1: 9 - 25; end oplasm ic - 28%; cy toplas mic - 20%; n uclear - 20%; - Golgi	TM= 1; TM domain 1: 9 - 25; end oplasm ic - 28%; cy toplas mic - 20%; n uclear - 20%; - Golgi	[Drosophila melanogaster] CG8340 product [QuerySize=367]	[Drosophila melanogaster] CG8340 product [QuerySize=367]			3.20E-145

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
115	SM, AS	Glycosyl transferase	N/A	TM= 0;	TMHMM =1; Inside 1 6; TMhelix 7 28; outside 30 377;	gi7282895 gb AAE442				4.10E-144

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interaction	PSCORE
116	Ab, SM, AS	transporter - ATP-binding	ABC_tran	TM= 5; TM domain outside 1: 413 -1 405; 429; T M 406 domain 428; 2: 442 -inside 458; T 429 M 440; domain TMhelix 3: 515 -441 531; T 463; M outside domain 464 4: 552 -486; 568; T TMhelix M 487 domain 509; 5: 637 -inside 653; pla 510 sma - 515; 40%; s TMhelix ndopla 516 smic - 538; 20%; m outside ltochon 539 drial - 547; 16%; TMhelix 548 570; inside	gi7286257 gb AAE619 51548.1 CG3164 gene product [Drosophila melanogaster] /QuerySize=619	619	ABC_tran		6.00E-181	

Row	Target type	Category	Motif H	Psort TM	TM HMM	Fly gene Acc	Fly aa	Motif Fly	Interact ion	PSCORE
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Row	Target Category	Motif H	Sort	TM	Fly gene Acc	Fly aa	Motif Fly	Interact	PSCORE
type			TM	HMM				ion	
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Row	Target Category	Motif H	Sort	TM	Fly gene Acc	Fly aa	Motif Fly	Interact	PSCORE
type			TM	HMM				ion	
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Table 2

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4503294	81	DDX3	HLP2	1	11	22	30	0
13651373	67	FLJ1209		0	3	4	30	0
3108194	72	HAPIP	DUO	0	11	1	30	0
7453574	64	HRMT1L2		1	3	5	30	0
7767238	41	IGSF4		1	3	2	25	0
3882220	88	KIAA0750		4	11	4	30	0
12742019	42	NFHS1		1	3	3	25	0
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12803124	96	U5-100K	PRP28	1	11	13	30	0
6010175	68	416221.5.2		0	3	3	26	14
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			LOC112806					
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11545923	232	ABCG4	WHITE2	0	3	4	25	0

WHAT IS CLAIMED IS:

1. A method of identifying a candidate p53 pathway modulating agent, said method comprising the steps of:
 - (a) providing an assay system comprising a purified HM polypeptide or nucleic acid or a functionally active fragment or derivative thereof;
 - (b) contacting the assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and
 - (c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate p53 pathway modulating agent.
2. The method of Claim 1 wherein the assay system comprises cultured cells that express the HM polypeptide.
3. The method of Claim 2 wherein the cultured cells additionally have defective p53 function.
4. The method of Claim 1 wherein the assay system includes a screening assay comprising a HM polypeptide, and the candidate test agent is a small molecule modulator.
5. The method of Claim 4 wherein the assay is a binding assay.
6. The method of Claim 1 wherein the assay system is selected from the group consisting of an apoptosis assay system, a cell proliferation assay system, an angiogenesis assay system, and a hypoxic induction assay system.
7. The method of Claim 1 wherein the assay system includes a binding assay comprising a HM polypeptide and the candidate test agent is an antibody.
8. The method of Claim 1 wherein the assay system includes an expression assay comprising a HM nucleic acid and the candidate test agent is a nucleic acid modulator.

9. The method of claim 8 wherein the nucleic acid modulator is an antisense oligomer.

10. The method of Claim 8 wherein the nucleic acid modulator is a PMO.

11. The method of Claim 1 additionally comprising:

(d) administering the candidate p53 pathway modulating agent identified in (c) to a model system comprising cells defective in p53 function and, detecting a phenotypic change in the model system that indicates that the p53 function is restored.

12. The method of Claim 11 wherein the model system is a mouse model with defective p53 function.

13. A method for modulating a p53 pathway of a cell comprising contacting a cell defective in p53 function with a candidate modulator that specifically binds to a HM polypeptide comprising an HM amino acid sequence, whereby p53 function is restored.

14. The method of claim 13 wherein the candidate modulator is administered to a vertebrate animal predetermined to have a disease or disorder resulting from a defect in p53 function.

15. The method of Claim 13 wherein the candidate modulator is selected from the group consisting of an antibody and a small molecule.

16. The method of Claim 1, comprising the additional steps of:

(d) providing a secondary assay system comprising cultured cells or a non-human animal expressing HM,

(e) contacting the secondary assay system with the test agent of (b) or an agent derived therefrom under conditions whereby, but for the presence of the test agent or agent derived therefrom, the system provides a reference activity; and

(f) detecting an agent-biased activity of the second assay system,

wherein a difference between the agent-biased activity and the reference activity of the second assay system confirms the test agent or agent derived therefrom as a candidate p53 pathway modulating agent,

and wherein the second assay detects an agent-biased change in the p53 pathway.

17. The method of Claim 16 wherein the secondary assay system comprises cultured cells.

18. The method of Claim 16 wherein the secondary assay system comprises a non-human animal.

19. The method of Claim 18 wherein the non-human animal mis-expresses a p53 pathway gene.

20. A method of modulating p53 pathway in a mammalian cell comprising contacting the cell with an agent that specifically binds a HM polypeptide or nucleic acid.

21. The method of Claim 20 wherein the agent is administered to a mammalian animal predetermined to have a pathology associated with the p53 pathway.

22. The method of Claim 20 wherein the agent is a small molecule modulator, a nucleic acid modulator, or an antibody.

23. A method for diagnosing a disease in a patient comprising:

(a) obtaining a biological sample from the patient;

(b) contacting the sample with a probe for HM expression;

(c) comparing results from step (b) with a control;

(d) determining whether step (c) indicates a likelihood of disease.

24. The method of claim 23 wherein said disease is cancer.

25. The method according to claim 24, wherein said cancer is a cancer as shown in Table 2 as having >25% expression level.

SEQUENCE LISTING

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14

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15

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16

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<212> DNA

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102

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134

135

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<210> 51

<211> 1964

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

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<210> 50

<211> 2091

<212> DNA

<213> Homo sapiens

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<210> 52

<211> 1955

<212> DNA

<213> Homo sapiens

<400> 52

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136

<211> 2187
 <212> DNA
 <213> Homo sapiens

<400> 53

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<211> 233

<212> DNA

<213> Homo sapiens

<400> 54

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<210> 55

<211> 5924

<212> DNA

<213> Homo sapiens

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137

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<210> 56

<211> 11145

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199

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<213> Homo sapiens

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209

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<212> DNA

<213> Homo sapiens

<400> 92

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<213> Homo sapiens

<400> 93

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213

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215

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<211> 893

<212> DNA

<213> Homo sapiens

<400> 106

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<211> 1015

<212> DNA

<213> Homo sapiens

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229

230

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<211> 1312

<212> DNA

<213> Homo sapiens

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<210> 109

<211> 3460

<212> DNA

<213> Homo sapiens

<400> 109

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 attctcga agttactat agctgattt gatctgaca gctatgga ctgtttgca 720
 aagtggaac gtctatga gacattgat aaccagtgta tggaggttg ttataaag 780
 ttaagtctg tcaattga aactgttg ttactatg aacgttgat gagaacactc 840
 ttaagttcc tcaattgca atgagacc tcagtattg acctagaa gatgattgg 900
 aagctgggg gagtgtctt gtcaaaagc gagagatca cagaccagt aacacagca 960
 gtaacatg gactctat aanaatgtt gggagatac cgcagatgt ttacagac 1020
 atgacagta tgtctctat ctgtccag ctgtgatag acctatgc caaccact 1080
 aactacgaa accctgaa caaatatt gaaacactc gaaggtcta tagcagaa 1140
 tccaactac ctgacttct taagaanaa cccagactg agcaagtga tggcagaa 1200
 caggagctc ttcatacat gaggaaagt tctgtcttt taccagagc gaaatctct 1260

<210> 116
 <211> 465
 <212> PRT
 <213> Homo sapiens

<400> 116
 Met Ile Val Phe Val Arg Phe Asn Ser Ser His Gly Phe Pro Val Glu 1
 1
 Val Asp Ser Asp Thr Ser Ile Phe Gln Leu Lys Glu Val Val Ala Lys 20
 20
 Arg Gln Gly Val Pro Ala Asp Gln Leu Arg Val Ile Phe Ala Gly Lys 35
 35

aggattagct gtcccctgac aucttgggtg gacgtctgc accitggctg cgcgcctgt 1320
 gatttgcca tttctctccc actgagaga tggaggtgtc cgcacagctt tgggctcgt 1380
 gaggatgct cctctctgac aaagagctct tgaaccgat tcatgaca ggcctcagt 1440
 aaggagcca gaagacaaat ggtttctgc ttaaaactc totgtcttc tttcttaca 1500
 tgaatcgtt ttttttaag tgggtgggtt aaaaatgga tctgttaag agactggg 1560
 agtctcctt tgaataagt tgtctgaca tttctaatg ttttgaaga cagctggg 1620
 ttttaagt ttttgaagt aataatta aatactaa ttatttaatt catttattg 1680
 tttctagaa gttgggaat taccattata catttacaat ctatgactt ttgtatttta 1740
 tttttcaaa taagagttt caatgga 1768

<210> 115
 <211> 1855
 <212> DNA
 <213> Homo sapiens

<400> 115
 ctgggtgctt ggggtgctt cgcggtctt cgcacgggc tctgcaaga gacagcttg 60
 gcaacagc acaaggctg gggccagag atgagctgc ccaaggaga tgtgagctg 120
 ggggtgctt cgttaactg tegtgaag ccaagagcg ggcctcagc ccaagctac 180
 cctgtctcg gccagcatg gctgtgctg tgcgagagt gctgtgga cccggctg 240
 cctgtgctt ggtgtgctg gttcagctg gacagagt gctagatgc cggcgctgc 300
 tggcggtct cgcagccc cgggggcca tgcgctga gcaggagag ctggtgatg 360
 tgggaccaa cagctgaaa taccgtatg gaaagcctt ggcactcact tctgtgggtg 420
 ggtgtgctt cagtgagc acgttgatg ggcagctg gacgcccac cccgagctg 480
 gctgagcg ggaagctgc atcatccgc ggtgtctgc catgcccag gctgtgcca 540
 agtctggcg tgaagctg cgtgtgatg agcggggtt gacgatgag tgtgtgacg 600
 cgcagcca ggcctcact ctagagtg tttcaaga cggagagcg gcccgctgc 660
 tctgacaaa ggaacctatt acgttaagt cctgtctta cctgtctc ctgtctcca 720
 actcaagt cctgtgatg gtggggag cgtgagctc cgtgagctc atgtacac 780
 gcaagcact caggtggag ttgactca cagctacgc tgaactgca accaagtgc 840
 ctgtacta cgaagctg gtgtgac caggcgctc actcaagct atctgact 900
 tccgtgct cgtctgag gacgtgct tccacatga agactcact ggaagcctg 960
 gtgtgtct cctgtcag atcgaggt ccaagacca ggtcatcag cctgttaac 1020
 tgaagcgt ctccagtg tccctgaca tccctgcca tgtgtgga gacatgctc 1140
 agatccgc catgtgct cagctgct atgacctt tgaaccca ccaactatg 1200
 gcaacctga cctctctc atcaacaa cagcggtgt cttgaagg ctaataaaa 1260
 caccagcaa tctgaagg tattttag gaaacagaa cagacctc tccccttag 1320
 gaagctgt atttccag ctccgcaat gactcatt ccaagagag aagaaatgc 1380
 atttaagt aaatggacc tctaacta gcatattgt tctattat cgcacaaa 1440
 ggaactga tgaagagt atttgcat gtttcaaaa gctgaact tgaagacta 1500
 cctgaact ctatactct ggaactcga ggttagaga tgaaggtat ggaagtgtc 1560
 ggtttttga aacttagta ttttatatt tcccctcaa gaacttttt ttaagaca 1620
 gatttgcat cctctaat ttgagagt gctgtgtg cttgtttgc tgggacag 1680
 cccacact gtgctctc tatgacct tacttgat tcaagaate tatttaag 1740
 ttttaatat gagcttct tgaatctc ctagtctta ctagtttca cagaggaaa 1800
 aaatctctt tgaataagt gaacagagc tcaattgtt gctctcact ttaca 1855

<210> 116
 <211> 465
 <212> PRT
 <213> Homo sapiens

<400> 116
 Met Ile Val Phe Val Arg Phe Asn Ser Ser His Gly Phe Pro Val Glu 1
 1
 Val Asp Ser Asp Thr Ser Ile Phe Gln Leu Lys Glu Val Val Ala Lys 20
 20
 Arg Gln Gly Val Pro Ala Asp Gln Leu Arg Val Ile Phe Ala Gly Lys 35
 35

Glu Leu Arg Asn Asp Trp Thr Val Gln Asn Cys Asp Leu Asp Gln Gln
50 55 60
Ser Ile Val His Ile Val Gln Arg Pro Trp Arg Lys Gly Gln Glu Met
65 70 75 80
Asn Ala Thr Gly Gly Asp Asp Pro Arg Asn Ala Ala Gly Gly Cys Glu
85 90 95
Arg Glu Pro Gln Ser Leu Thr Arg Val Asp Leu Ser Ser Val Leu
100 105 110
Pro Gly Asp Ser Val Gly Leu Ala Val Ile Leu His Thr Asp Ser Arg
115 120 125
Lys Asp Ser Pro Pro Ala Gly Ser Pro Ala Gly Arg Ser Ile Tyr Asn
130 135 140
Ser Phe Tyr Val Tyr Cys Lys Gly Pro Cys Gln Arg Val Gln Pro Gly
145 150 155 160
Lys Leu Arg Val Gln Cys Ser Thr Cys Arg Gln Ala Thr Leu Thr Leu
165 170 175
Thr Gln Gly Pro Ser Cys Trp Asp Asp Val Leu Ile Pro Asn Arg Met
180 185 190
Ser Gly Glu Cys Gln Ser Pro His Cys Pro Gly Thr Ser Ala Glu Phe
195 200 205
Phe Phe Lys Cys Gly Ala His Pro Thr Ser Asp Lys Glu Thr Pro Val
210 215 220
Ala Leu His Leu Ile Ala Thr Asn Ser Arg Asn Ile Thr Cys Ile Thr
225 230 235 240
Cys Thr Asp Val Arg Ser Pro Val Leu Val Phe Gln Cys Asn Ser Arg
245 250 255
His Val Ile Cys Leu Asp Cys Phe His Leu Tyr Cys Val Thr Arg Leu
260 265 270
Asn Asp Arg Gln Phe Val His Asp Pro Gln Leu Gly Tyr Ser Leu Pro
275 280 285
Cys Val Ala Gly Cys Pro Asn Ser Leu Ile Lys Glu Leu His His Phe
290 295 300
Arg Ile Leu Gly Glu Gln Tyr Asn Arg Tyr Gln Gln Tyr Gly Ala
305 310 315 320
Glu Glu Cys Val Leu Gln Met Gly Gly Val Leu Cys Pro Arg Pro Gly
325 330 335
Cys Gly Ala Gly Leu Leu Pro Glu Pro Asp Gln Arg Lys Val Thr Cys
340 345 350
Glu Gly Asn Gly Leu Gly Cys Gly Phe Ala Phe Cys Arg Glu Cys
355 360 365
Lys Glu Ala Tyr His Glu Gly Glu Cys Ser Ala Val Phe Glu Ala Ser

235

370 375 380
Gly Thr Thr Thr Gln Ala Tyr Arg Val Asp Glu Arg Ala Ala Glu Gln
385 390 395 400
Ala Arg Trp Glu Ala Ala Ser Lys Glu Thr Ile Lys Lys Thr Thr Lys
405 410 415
Pro Cys Pro Arg Cys His Val Pro Val Glu Lys Asn Gly Gly Cys Met
420 425 430
His Met Lys Cys Pro Gln Pro Gln Cys Arg Leu Glu Trp Cys Trp Asn
435 440 445
Cys Gly Cys Glu Trp Asn Arg Val Cys Met Gly Asp His Trp Phe Asp
450 455 460
Val
465
<210> 117
<211> 437
<212> PRT
<213> Homo sapiens
<400> 117
Met Ile Val Phe Val Arg Phe Asn Ser Ser His Gly Phe Pro Val Glu
1 5 10 15
Val Asp Ser Asp Thr Ser Ile Phe Gln Leu Lys Glu Val Val Ala Lys
20 25 30
Arg Gln Gly Val Pro Ala Asp Gln Leu Arg Val Ile Phe Ala Gly Lys
35 40 45
Glu Leu Arg Asn Asp Trp Thr Val Gln Asn Cys Asp Leu Asp Gln Gln
50 55 60
Ser Ile Val His Ile Val Gln Arg Pro Trp Arg Lys Gly Gln Glu Met
65 70 75 80
Asn Ala Thr Gly Gly Asp Asp Pro Arg Asn Ala Ala Gly Gly Cys Glu
85 90 95
Arg Glu Pro Gln Ser Leu Thr Arg Val Asp Leu Ser Ser Val Leu
100 105 110
Pro Gly Asp Ser Val Gly Leu Ala Val Ile Leu His Thr Asp Ser Arg
115 120 125
Lys Asp Ser Pro Pro Ala Gly Ser Pro Ala Gly Arg Ser Ile Tyr Asn
130 135 140
Ser Phe Tyr Val Tyr Cys Lys Gly Pro Cys Gln Arg Val Gln Pro Gly
145 150 155 160
Lys Leu Arg Val Gln Cys Ser Thr Cys Arg Gln Ala Thr Leu Thr Leu
165 170 175
Thr Gln Glu Phe Phe Lys Cys Gly Ala His Pro Thr Ser Asp Lys
180 185 190

236

Glu Thr Pro Val Ala Leu His Leu Ile Ala Thr Asn Ser Arg Asn Ile
 195 200 205
 Thr Cys Ile Thr Cys Thr Asp Val Arg Ser Pro Val Leu Val Phe Gln
 210 215 220
 Cys Asn Ser Arg His Val Ile Cys Leu Asp Cys Phe His Leu Tyr Cys
 225 230 235 240
 Val Thr Arg Leu Asn Asp Arg Gln Phe Val His Asp Pro Gln Leu Gly
 245 250 255
 Tyr Ser Leu Pro Cys Val Ala Gly Cys Pro Asn Ser Leu Ile Lys Glu
 260 265 270
 Leu His His Phe Arg Ile Leu Gly Glu Gln Tyr Asn Arg Tyr Gln
 275 280 285
 Gln Tyr Gly Ala Glu Glu Cys Val Leu Gln Met Gly Val Leu Cys
 290 295 300
 Pro Arg Pro Gly Cys Gly Ala Gly Leu Leu Pro Glu Pro Asp Gln Arg
 305 310 315 320
 Lys Val Thr Cys Glu Gly Gly Asn Gly Leu Gly Cys Gly Phe Ala Phe
 325 330 335
 Cys Arg Glu Cys Lys Glu Ala Tyr His Glu Gly Glu Cys Ser Ala Val
 340 345 350
 Phe Glu Ala Ser Gly Thr Thr Gln Ala Tyr Arg Val Asp Glu Arg
 355 360 365
 Ala Ala Glu Gln Ala Arg Trp Glu Ala Ala Ser Lys Glu Thr Ile Lys
 370 375 380
 Lys Thr Thr Lys Pro Cys Pro Arg Cys His Val Pro Val Glu Lys Asn
 385 390 395 400
 Gly Gly Cys Met His Met Lys Cys Pro Gln Pro Gln Cys Arg Leu Glu
 405 410 415
 Trp Cys Trp Asn Cys Gly Cys Glu Trp Asn Arg Val Cys Met Gly Asp
 420 425 430
 His Trp Phe Asp Val
 435
 <210> 118
 <211> 316
 <212> PRT
 <213> Homo sapiens
 <400> 118
 Met Ile Val Phe Val Arg Phe Asn Ser Ser His Gly Phe Pro Val Glu
 1 5 10 15
 Val Asp Ser Asp Thr Ser Ile Phe Gln Leu Lys Glu Val Val Ala Lys
 20 25 30
 Arg Gln Gly Val Pro Ala Asp Gln Leu Arg Val Ile Phe Ala Gly Lys
 35 40 45

Glu Leu Arg Asn Asp Trp Thr Val Gln Glu Phe Phe Lys Cys Gly
 50 55 60
 Ala His Pro Thr Ser Asp Lys Glu Thr Pro Val Ala Leu His Leu Ile
 65 70 75 80
 Ala Thr Asn Ser Arg Asn Ile Thr Cys Ile Thr Cys Thr Asp Val Arg
 85 90 95
 Ser Pro Val Leu Val Phe Gln Cys Asn Ser Arg His Val Ile Cys Leu
 100 105 110
 Asp Cys Phe His Leu Tyr Cys Val Thr Arg Leu Asn Asp Arg Gln Phe
 115 120 125
 Val His Asp Pro Gln Leu Gly Tyr Ser Leu Pro Cys Val Ala Gly Cys
 130 135 140
 Pro Asn Ser Leu Ile Lys Glu Leu His Phe Arg Ile Leu Gly Glu
 145 150 155 160
 Glu Gln Tyr Asn Arg Tyr Gln Gln Tyr Gly Ala Glu Glu Cys Val Leu
 165 170 175
 Gln Met Gly Gly Val Leu Cys Pro Arg Pro Gly Cys Gly Ala Gly Leu
 180 185 190
 Leu Pro Glu Pro Asp Gln Arg Lys Val Thr Cys Glu Gly Gly Asn Gly
 195 200 205
 Leu Gly Cys Gly Phe Ala Phe Cys Arg Glu Cys Lys Glu Ala Tyr His
 210 215 220
 Glu Gly Glu Cys Ser Ala Val Phe Glu Ala Ser Gly Thr Thr Thr Gln
 225 230 235 240
 Ala Tyr Arg Val Asp Glu Arg Ala Ala Glu Gln Ala Arg Trp Glu Ala
 245 250 255
 Ala Ser Lys Glu Thr Ile Lys Lys Thr Thr Lys Pro Cys Pro Arg Cys
 260 265 270
 His Val Pro Val Glu Lys Asn Gly Gly Cys Met His Met Lys Cys Pro
 275 280 285
 Gln Pro Gln Cys Arg Leu Glu Trp Cys Trp Asn Cys Gly Cys Glu Trp
 290 295 300
 Asn Arg Val Cys Met Gly Asp His Trp Phe Asp Val
 305 310 315
 <210> 119
 <211> 534
 <212> PRT
 <213> Homo sapiens
 <400> 119
 Met Ile Trp Tyr Ile Leu Ile Ile Gly Ile Leu Leu Pro Gln Ser Leu
 1 5 10 15
 Ala His Pro Gly Phe Thr Ser Ile Gly Gln Met Thr Asp Leu Ile

20 25 30
 His Thr Glu Lys Asp Leu Val Thr Ser Leu Lys Asp Tyr Ile Lys Ala 45
 35
 Glu Glu Asp Lys Leu Glu Gln Ile Lys Lys Trp Ala Glu Lys Leu Asp 60
 50 55
 Arg Leu Thr Ser Thr Ala Thr Lys Asp Pro Glu Gly Phe Val Gly His 75
 65 70
 Pro Val Asn Ala Phe Lys Leu Met Lys Arg Leu Asn Thr Glu Trp Ser 90
 85 95
 Glu Leu Glu Asn Leu Val Leu Lys Asp Met Ser Asp Gly Phe Ile Ser 110
 100 105
 Asn Leu Thr Ile Gln Arg Pro Val Leu Ser Asn Asp Glu Asp Gln Val 125
 115 120
 Gly Ala Ala Lys Ala Leu Leu Arg Leu Gln Asp Thr Tyr Asn Leu Asp 140
 130 135
 Thr Asp Thr Ile Ser Lys Gly Asn Leu Pro Gly Val Lys His Lys Ser 155
 145 150
 Phe Leu Thr Ala Glu Asp Cys Phe Glu Leu Gly Lys Val Ala Tyr Thr 175
 165 170
 Glu Ala Asp Tyr Tyr His Thr Glu Leu Trp Met Glu Gln Ala Leu Arg 190
 180 185
 Gln Leu Asp Glu Gly Glu Ile Ser Thr Ile Asp Lys Val Ser Val Leu 205
 195 200
 Asp Tyr Leu Ser Tyr Ala Val Tyr Gln Gln Gly Asp Leu Asp Lys Ala 220
 210 215
 Leu Leu Leu Thr Lys Lys Leu Leu Glu Leu Asp Pro Glu His Gln Arg 240
 225 230 235
 Ala Asn Gly Asn Leu Lys Tyr Phe Glu Tyr Ile Met Ala Lys Glu Lys 255
 245 250
 Asp Val Asn Lys Ser Ala Ser Asp Asp Gln Ser Asp Gln Lys Thr Thr 270
 260 265
 Pro Lys Lys Lys Gly Val Ala Val Asp Tyr Leu Pro Glu Arg Gln Lys 285
 275 280
 Tyr Glu Met Leu Cys Arg Gly Glu Gly Ile Lys Met Thr Pro Arg Arg 300
 290 295
 Gln Lys Lys Leu Phe Cys Arg Tyr His Asp Gly Asn Arg Asn Pro Lys 320
 305 310 315
 Phe Ile Leu Ala Pro Ala Lys Gln Glu Asp Glu Trp Asp Lys Pro Arg 335
 325 330
 Ile Ile Arg Phe His Asp Ile Ile Ser Asp Ala Glu Ile Glu Ile Val 350
 340 345

239

Lys Asp Leu Ala Lys Pro Arg Leu Arg Arg Ala Thr Ile Ser Asn Pro 365
 355 360
 Ile Thr Gly Asp Leu Glu Thr Val His Tyr Arg Ile Ser Lys Ser Ala 380
 370 375
 Trp Leu Ser Gly Tyr Glu Asn Pro Val Val Ser Arg Ile Asn Met Arg 400
 385 390 395
 Ile Gln Asp Leu Thr Gly Leu Asp Val Ser Thr Ala Glu Glu Leu Gln 415
 405 410
 Val Ala Asn Tyr Gly Val Gly Gln Tyr Glu Pro His Phe Asp Phe 430
 420 425
 Ala Arg Lys Asp Glu Pro Asp Ala Phe Lys Glu Leu Gly Thr Gly Asn 445
 435 440
 Arg Ile Ala Thr Trp Leu Phe Tyr Met Ser Asp Val Ser Ala Gly Gly 460
 450 455
 Ala Thr Val Phe Pro Glu Val Gly Ala Ser Val Trp Pro Lys Lys Gly 480
 465 470 475
 Thr Ala Val Phe Trp Tyr Asn Leu Phe Ala Ser Gly Glu Gly Asp Tyr 495
 485 490
 Ser Thr Arg His Ala Ala Cys Pro Val Leu Val Gly Asn Lys Trp Val 510
 500 505
 Ser Asn Lys Trp Leu His Glu Arg Gly Gln Glu Phe Arg Arg Pro Cys 525
 515 520
 Thr Leu Ser Glu Leu Glu 530
 530
 <210> 120
 <211> 535
 <212> PRT
 <213> Homo sapiens
 <400> 120
 Met Lys Leu Trp Val Ser Ala Leu Leu Met Ala Trp Phe Gly Val Leu 15
 1 5 10
 Ser Cys Val Gln Ala Glu Phe Phe Thr Ser Ile Gly His Met Thr Asp 30
 20 25
 Leu Ile Tyr Ala Glu Lys Glu Leu Val Gln Ser Leu Lys Glu Tyr Ile 45
 35 40
 Leu Val Glu Glu Ala Lys Leu Ser Lys Ile Lys Ser Trp Ala Asn Lys 60
 50 55
 Met Glu Ala Leu Thr Ser Lys Ser Ala Asp Ala Glu Gly Tyr Leu 80
 65 70 75
 Ala His Pro Val Asn Ala Tyr Lys Leu Val Lys Arg Leu Asn Thr Asp 95
 85 90
 Trp Pro Ala Leu Glu Asp Leu Val Leu Gln Asp Ser Ala Ala Gly Phe 110
 100 105

240

Ile Ala Asn Leu Ser Val Gln Arg Gln Phe Pro Thr Asp Glu Asp
115 120 125
Glu Ile Gly Ala Ala Lys Ala Leu Met Arg Leu Gln Asp Thr Tyr Arg
130 135 140 145
Leu Asp Pro Gly Thr Ile Ser Arg Gly Glu Leu Pro Gly Thr Lys Tyr
145 150 155 160
Gln Ala Met Leu Ser Val Asp Asp Cys Phe Gly Met Gly Arg Ser Ala
165 170 175
Tyr Asn Glu Gly Asp Tyr Tyr His Thr Val Leu Trp Met Glu Gln Val
180 185 190
Leu Lys Gln Leu Asp Ala Gly Glu Glu Ala Thr Thr Lys Ser Gln
195 200 205
Val Leu Asp Tyr Leu Ser Tyr Ala Val Phe Gln Leu Gly Asp Leu His
210 215 220
Arg Ala Leu Glu Leu Thr Arg Arg Leu Ser Leu Asp Pro Ser His
225 230 235 240
Glu Arg Ala Gly Asn Leu Arg Tyr Phe Glu Gln Leu Leu Glu Glu
245 250 255
Glu Arg Glu Lys Thr Leu Thr Asn Gln Thr Glu Ala Glu Leu Ala Thr
260 265 270
Pro Glu Gly Ile Tyr Glu Arg Pro Val Asp Tyr Leu Pro Glu Arg Asp
275 280 285
Val Tyr Glu Ser Leu Cys Arg Gly Glu Gly Val Lys Leu Thr Pro Arg
290 295 300
Arg Gln Lys Arg Leu Phe Cys Arg Tyr His His Gly Asn Arg Ala Pro
305 310 315 320
Gln Leu Leu Ile Ala Pro Phe Lys Glu Asp Glu Trp Asp Ser Pro
325 330 335
His Ile Val Arg Tyr Tyr Asp Val Met Ser Asp Glu Glu Ile Glu Arg
340 345 350
Ile Lys Glu Ile Ala Lys Pro Lys Leu Ala Arg Ala Thr Val Arg Asp
355 360 365
Pro Lys Thr Gly Val Leu Thr Val Ala Ser Tyr Arg Val Ser Lys Ser
370 375 380
Ser Trp Leu Glu Glu Asp Asp Asp Pro Val Val Ala Arg Val Asn Arg
385 390 395 400
Arg Met Gln His Ile Thr Gly Leu Thr Val Lys Thr Ala Glu Leu Leu
405 410 415
Gln Val Ala Asn Tyr Gly Val Gly Gly Gln Tyr Glu Pro His Phe Asp
420 425 430
Phe Ser Arg Asn Asp Glu Arg Asp Thr Phe Lys His Leu Gly Thr Gly

241

Asn Arg Val Ala Thr Phe Leu Asn Tyr Met Ser Asp Val Glu Ala Gly
435 440 445 450 455
Gly Ala Thr Val Phe Pro Asp Leu Gly Ala Ala Ile Trp Pro Lys Lys
465 470 475 480
Gly Thr Ala Val Phe Trp Tyr Asn Leu Leu Arg Ser Gly Glu Gly Asp
485 490 495
Tyr Arg Thr Arg His Ala Ala Cys Pro Val Leu Val Gly Cys Lys Trp
500 505 510
Val Ser Asn Lys Trp Phe His Glu Arg Gly Gln Glu Phe Leu Arg Pro
515 520 525
Cys Gly Ser Thr Glu Val Asp
530 535
<210> 121
<211> 524
<212> PRT
<213> Homo sapiens
<400> 121
Met Phe His Cys Ile Pro Leu Trp Arg Cys Asn Arg His Val Glu Ser
1 5 10 15
Ile Asp Lys Arg His Cys Ser Leu Val Tyr Val Pro Glu Glu Ile Tyr
20 25 30
Arg Tyr Ala Arg Ser Leu Glu Glu Leu Leu Asp Ala Asn Gln Leu
35 40 45
Arg Glu Leu Pro Glu Gln Phe Phe Gln Leu Val Lys Leu Arg Lys Leu
50 55 60
Gly Leu Ser Asp Asn Glu Ile Gln Arg Leu Pro Pro Glu Ile Ala Asn
65 70 75 80
Phe Met Gln Leu Val Glu Leu Asp Val Ser Arg Asn Glu Ile Pro Glu
85 90 95
Ile Pro Glu Ser Ile Ser Phe Cys Lys Ala Leu Gln Val Ala Asp Phe
100 105 110
Ser Gly Asn Pro Leu Thr Arg Leu Pro Glu Ser Phe Pro Glu Leu Gln
115 120 125
Asn Leu Thr Cys Leu Ser Val Asn Asp Ile Ser Leu Gln Ser Leu Pro
130 135 140
Glu Asn Ile Gly Asn Leu Tyr Asn Leu Ala Ser Leu Glu Leu Arg Glu
145 150 155 160
Asn Leu Leu Thr Tyr Leu Pro Asp Ser Leu Thr Gln Leu Arg Arg Leu
165 170 175
Glu Glu Leu Asp Leu Gly Asn Asn Glu Ile Tyr Asn Leu Pro Glu Ser
180 185 190

242

Ile Gly Ala Leu Leu His Leu Lys Asp Leu Trp Leu Asp Gly Asn Gln
195 200 205

Leu Ser Glu Leu Pro Gln Glu Ile Gly Asn Leu Lys Asn Leu Cys
210 215 220

Leu Asp Val Ser Glu Asn Arg Leu Glu Arg Leu Pro Glu Glu Ile Ser
235 230 235 240

Gly Leu Thr Ser Leu Thr Asp Leu Val Ile Ser Gln Asn Leu Glu
245 250 255

Thr Ile Pro Asp Gly Ile Gly Lys Leu Lys Lys Leu Ser Ile Leu Lys
260 265 270

Val Asp Gln Asn Arg Leu Thr Gln Leu Pro Glu Ala Val Gly Glu Cys
275 280 285

Glu Ser Leu Thr Glu Leu Val Leu Thr Glu Asn Gln Leu Thr Leu
290 295 300

Pro Lys Ser Ile Gly Lys Leu Lys Lys Leu Ser Asn Leu Asn Ala Asp
305 310 315 320

Arg Asn Lys Leu Val Ser Leu Pro Lys Glu Ile Gly Gly Cys Ser
325 330 335

Leu Thr Val Phe Cys Val Arg Asp Asn Arg Leu Thr Arg Ile Pro Ala
340 345 350

Glu Val Ser Gln Ala Thr Glu Leu His Val Leu Asp Val Ala Gly Asn
355 360 365

Arg Leu Leu His Leu Pro Leu Ser Leu Thr Ala Leu Lys Leu Lys Ala
370 375 380

Leu Trp Leu Ser Asp Asn Gln Ser Gln Pro Leu Leu Thr Phe Gln Thr
385 390 395 400

Asp Thr Asp Tyr Thr Thr Gly Glu Lys Ile Leu Thr Cys Val Leu Leu
405 410 415

Pro Gln Leu Pro Ser Glu Pro Thr Cys Gln Glu Asn Leu Pro Arg Cys
420 425 430

Gly Ala Leu Glu Asn Leu Val Asn Asp Val Ser Asp Glu Ala Trp Asn
435 440 445

Glu Arg Ala Val Asn Arg Val Ser Ala Ile Arg Phe Val Glu Asp Glu
450 455 460

Lys Asp Glu Glu Asp Asn Glu Thr Arg Thr Leu Leu Arg Arg Ala Thr
465 470 475 480

Pro His Pro Gly Glu Leu Lys His Met Lys Lys Thr Val Glu Asn Leu
485 490 495

Arg Asn Asp Met Asn Ala Ala Lys Gly Leu Asp Ser Asn Lys Asn Glu
500 505 510

Val Asn His Ala Ile Asp Arg Val Thr Thr Ser Val
515 520

<210> 122
<211> 1551
<212> PRT
<213> Homo sapiens

<400> 122
Ser Asp Asn Glu Ile Gln Arg Leu Pro Pro Glu Val Ala Asn Phe Met
1 5 10 15

Gln Leu Val Glu Leu Asp Val Ser Arg Asn Asp Ile Pro Glu Ile Pro
20 25 30

Glu Ser Ile Lys Phe Cys Lys Ala Leu Glu Ile Ala Asp Phe Ser Gly
35 40 45

Asn Pro Leu Ser Arg Leu Pro Asp Gly Phe Thr Gln Leu Arg Ser Leu
50 55 60

Ala His Leu Ala Leu Asn Asp Val Ser Leu Gln Ala Leu Pro Gly Asp
65 70 75 80

Val Gly Asn Leu Ala Asn Leu Val Thr Leu Glu Leu Arg Glu Asn Leu
85 90 95

Leu Lys Ser Leu Pro Ala Ser Leu Ser Phe Leu Val Lys Leu Glu Gln
100 105 110

Leu Asp Leu Gly Gly Asn Asp Leu Glu Val Leu Pro Asp Thr Leu Gly
115 120 125

Ala Leu Pro Asn Leu Arg Glu Leu Trp Leu Asp Arg Asn Gln Leu Ser
130 135 140

Ala Leu Pro Pro Glu Leu Gly Asn Leu Arg Arg Leu Val Cys Leu Asp
145 150 155 160

Val Ser Glu Asn Arg Leu Glu Glu Leu Pro Ala Glu Leu Gly Gly Leu
165 170 175

Val Leu Leu Thr Asp Leu Leu Ser Gln Asn Leu Leu Arg Arg Leu
180 185 190

Pro Asp Gly Ile Gly Gln Leu Lys Gln Leu Ser Ile Leu Lys Val Asp
195 200 205

Gln Asn Arg Leu Cys Glu Val Thr Glu Ala Ile Gly Asp Cys Glu Asn
210 215 220

Leu Ser Glu Leu Ile Leu Thr Glu Asn Leu Leu Met Ala Leu Pro Arg
225 230 235 240

Ser Leu Gly Lys Leu Thr Lys Leu Thr Asn Leu Asn Val Asp Arg Asn
245 250 255

His Leu Glu Ala Leu Pro Glu Ile Gly Gly Cys Val Ala Leu Ser
260 265 270

Val Leu Ser Leu Arg Asp Asn Arg Leu Ala Val Leu Pro Pro Glu Leu
275 280 285

Ala His Thr Thr Glu Leu His Val Leu Asp Val Ala Gly Asn Arg Leu
290 295 300

290 295 300
 Gln Ser Leu Pro Phe Ala Leu Thr His Leu Asn Leu Lys Ala Leu Trp 320
 305 310 315
 Leu Ala Glu Asn Gln Ala Gln Pro Met Leu Arg Phe Gln Thr Glu Asp 335
 325 330
 Asp Ala Arg Thr Gly Glu Lys Val Leu Thr Cys Tyr Leu Leu Pro Gln 350
 340 345
 Gln Pro Pro Leu Ser Leu Glu Asp Ala Gly Gln Gln Gly Ser Leu Ser 365
 355 360
 Glu Thr Trp Ser Asp Ala Pro Pro Ser Arg Val Ser Val Ile Gln Phe 380
 370 375
 Leu Glu Ala Pro Ile Gly Asp Glu Asp Ala Glu Glu Ala Ala Glu 400
 385 390 395
 Lys Arg Gly Leu Gln Arg Arg Ala Thr Pro His Pro Ser Glu Leu Lys 415
 405 410
 Val Met Lys Arg Ser Ile Glu Gly Arg Arg Ser Glu Ala Cys Pro Cys 430
 420 425
 Gln Pro Asp Ser Gly Ser Pro Leu Pro Ala Glu Glu Glu Lys Arg Leu 445
 435 440
 Ser Ala Glu Ser Gly Leu Ser Glu Asp Ser Arg Pro Ser Ala Ser Thr 460
 450 455
 Val Ser Glu Ala Glu Pro Glu Gly Pro Ser Ala Glu Ala Gln Gly Gly 480
 465 470 475
 Ser Gln Gln Glu Ala Thr Thr Ala Gly Gly Glu Glu Asp Ala Glu Glu 495
 485 490
 Asp Tyr Gln Glu Pro Thr Val His Phe Ala Glu Asp Ala Leu Leu Pro 510
 500 505
 Gly Asp Asp Arg Glu Ile Glu Glu Gly Gln Pro Glu Ala Pro Trp Thr 525
 515 520
 Leu Pro Gly Gly Arg Gln Arg Leu Ile Arg Lys Asp Thr Pro His Tyr 540
 530 535
 Lys Lys His Phe Lys Ile Ser Lys Leu Pro Gln Pro Glu Ala Val Val 560
 545 550 555
 Ala Leu Leu Gln Gly Met Gln Pro Asp Gly Glu Gly Pro Val Ala Pro 575
 565 570
 Gly Gly Trp His Asn Gly Pro His Ala Pro Trp Ala Pro Arg Ala Gln 590
 580 585
 Lys Glu Glu Glu Glu Glu Glu Gly Ser Pro Gln Glu Glu Glu Glu 605
 595 600
 Glu Glu Glu Glu Glu Asn Arg Ala Glu Glu Glu Ala Ser Thr Glu 620
 610 615

Glu Glu Asp Lys Glu Gly Ala Val Val Ser Ala Pro Ser Val Lys Gly 640
 625 630 635
 Val Ser Phe Asp Gln Ala Asn Asn Leu Leu Ile Glu Pro Ala Arg Ile 655
 645 650
 Glu Glu Glu Glu Leu Thr Leu Thr Ile Leu Arg Gln Thr Gly Gly Leu 670
 660 665
 Gly Ile Ser Ile Ala Gly Gly Lys Gly Ser Thr Pro Tyr Lys Gly Asp 685
 675 680
 Asp Glu Gly Ile Phe Ile Ser Arg Val Ser Glu Glu Gly Pro Ala Ala 700
 690 695
 Arg Ala Gly Val Arg Val Gly Asp Lys Leu Leu Glu Val Asn Gly Val 720
 705 710 715
 Ala Leu Gln Gly Ala Glu His His Glu Ala Val Glu Ala Leu Arg Gly 735
 725 730
 Ala Gly Thr Ala Val Gln Met Arg Val Trp Arg Glu Arg Met Val Glu 750
 740 745
 Pro Glu Asn Ala Val Thr Ile Thr Pro Leu Arg Pro Glu Asp Asp Tyr 765
 755 760
 Ser Pro Arg Glu Arg Arg Gly Gly Leu Arg Leu Pro Leu Leu Pro 780
 770 775
 Pro Glu Ser Pro Gly Pro Leu Arg Gln Arg His Val Ala Cys Leu Ala 800
 785 790 795
 Arg Ser Glu Arg Gly Leu Gly Phe Ser Ile Ala Gly Gly Lys Gly Ser 815
 805 810
 Thr Pro Tyr Arg Ala Gly Asp Ala Gly Ile Phe Val Ser Arg Ile Ala 830
 820 825
 Glu Gly Gly Ala Ala His Arg Ala Gly Thr Leu Gln Val Gly Asp Arg 845
 835 840
 Val Leu Ser Ile Asn Gly Val Asp Val Thr Glu Ala Arg His Asp His 860
 850 855
 Ala Val Ser Leu Leu Thr Ala Ala Ser Pro Thr Ile Ala Leu Leu Leu 880
 865 870 875
 Glu Arg Glu Ala Gly Gly Pro Leu Pro Pro Ser Pro Leu Pro His Ser 895
 885 890
 Ser Pro Pro Thr Ala Ala Val Ala Thr Thr Ser Ile Thr Thr Ala Thr 910
 900 905
 Pro Gly Val Pro Gly Leu Pro Ser Leu Ala Pro Ser Leu Leu Ala Ala 925
 915 920
 Ala Leu Glu Gly Pro Tyr Pro Val Glu Glu Ile Arg Leu Pro Arg Ala 940
 930 935
 Gly Gly Pro Leu Gly Leu Ser Ile Val Gly Gly Ser Asp His Ser Ser 960
 945 950 955

His Pro Phe Gly Val Gln Glu Pro Gly Val Phe Ile Ser Lys Val Leu 965 970 975
 Pro Arg Gly Leu Ala Ala Arg Ser Gly Leu Arg Val Gly Asp Arg Ile 980 985 990
 Leu Ala Val Asn Gly Gln Asp Val Arg Asp Ala Thr His Gln Glu Ala 995 1000 1005
 Val Ser Ala Leu Leu Arg Pro Cys Leu Glu Leu Ser Leu Leu Val 1010 1015 1020
 Arg Arg Asp Pro Ala Pro Pro Gly Leu Arg Glu Leu Cys Ile Gln 1025 1030 1035
 Lys Ala Pro Gly Glu Arg Leu Gly Ile Ser Ile Arg Gly Gly Ala 1040 1045 1050
 Arg Gly His Ala Gly Asn Pro Arg Asp Pro Thr Asp Glu Gly Ile 1055 1060 1065
 Phe Ile Ser Lys Val Ser Pro Thr Gly Ala Ala Gly Arg Asp Gly 1070 1075 1080
 Arg Leu Arg Val Gly Leu Arg Leu Leu Glu Val Asn Gln Gln Ser 1085 1090 1095
 Leu Leu Gly Leu Thr His Gly Glu Ala Val Gln Leu Leu Arg Ser 1100 1105 1110
 Val Gly Asp Thr Leu Thr Val Leu Val Cys Asp Gly Phe Glu Ala 1115 1120 1125
 Ser Thr Asp Ala Ala Leu Glu Val Ser Pro Gly Val Ile Ala Asn 1130 1135 1140
 Pro Phe Ala Ala Gly Ile Gly His Arg Asn Ser Leu Glu Ser Ile 1145 1150 1155
 Ser Ser Ile Asp Arg Glu Leu Ser Pro Glu Gly Pro Gly Lys Glu 1160 1165 1170
 Lys Glu Leu Pro Gly Gln Thr Leu His Trp Gly Pro Glu Ala Thr 1175 1180 1185
 Glu Ala Ala Gly Arg Gly Leu Gln Pro Leu Lys Leu Asp Tyr Arg 1190 1195 1200
 Ala Leu Ala Ala Val Pro Ser Ala Gly Ser Val Gln Arg Val Pro 1205 1210 1215
 Ser Gly Ala Ala Gly Gly Lys Met Ala Glu Ser Pro Cys Ser Pro 1220 1225 1230
 Ser Gly Gln Gln Pro Pro Ser Pro Pro Ser Pro Asp Glu Leu Pro 1235 1240 1245
 Ala Asn Val Lys Gln Ala Tyr Arg Ala Phe Ala Ala Val Pro Thr 1250 1255 1260
 Ser His Pro Pro Glu Asp Ala Pro Ala Gln Pro Thr Pro Gly 1265 1270 1275

1265 1270 1275
 Pro Ala Ala Ser Pro Glu Gln Leu Ser Phe Arg Glu Arg Gln Lys 1280 1285 1290
 Tyr Phe Glu Leu Glu Val Arg Val Pro Gln Ala Glu Gly Pro Pro 1295 1300 1305
 Lys Arg Val Ser Leu Val Gly Ala Asp Asp Leu Arg Lys Met Gln 1310 1315 1320
 Glu Glu Ala Arg Lys Leu Gln Gln Lys Arg Ala Gln Met Leu 1325 1330 1335
 Arg Glu Ala Ala Glu Ala Gly Ala Glu Ala Arg Leu Ala Leu Asp 1340 1345 1350
 Gly Glu Thr Leu Gly Glu Glu Gln Glu Asp Glu Gln Pro Pro 1355 1360 1365
 Trp Ala Ser Pro Ser Pro Thr Ser Arg Gln Ser Pro Ala Ser Pro 1370 1375 1380
 Pro Pro Leu Gly Gly Gly Ala Pro Val Arg Thr Ala Lys Ala Glu 1385 1390 1395
 Arg Arg His Gln Glu Arg Leu Arg Val Gln Ser Pro Glu Pro Pro 1400 1405 1410
 Ala Pro Glu Arg Ala Leu Ser Pro Ala Glu Leu Arg Ala Leu Glu 1415 1420 1425
 Ala Glu Lys Arg Ala Leu Trp Arg Ala Ala Arg Met Lys Ser Leu 1430 1435 1440
 Glu Gln Asp Ala Leu Arg Ala Gln Met Val Leu Ser Arg Ser Gln 1445 1450 1455
 Glu Gly Arg Gly Thr Arg Gly Pro Leu Glu Arg Leu Ala Glu Ala 1460 1465 1470
 Pro Ser Pro Ala Pro Thr Ser Pro Thr Pro Val Glu Asp Leu 1475 1480 1485
 Gly Pro Gln Thr Ser Thr Ser Pro Gly Arg Leu Ser Pro Asp Phe 1490 1495 1500
 Ala Glu Glu Leu Arg Ser Leu Glu Pro Ser Pro Ser Pro Gly Pro 1505 1510 1515
 Gln Arg Arg Met Glu Lys Trp Leu Trp Cys Phe Trp Ala Gly Pro 1520 1525 1530
 His Pro Ala Leu Trp Ala Leu Lys Met Trp His Cys Ala Ala Ala 1535 1540 1545
 Ala Ala Pro 1550
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 <211> 1371
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<213> Homo sapiens

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35 40 45
Glu Glu Leu Tyr Leu Asp Ala Asn Gln Ile Glu Glu Leu Pro Lys Gln
50 55 60
Leu Phe Asn Cys Gln Ser Leu His Lys Leu Ser Leu Pro Asp Asn Asp
65 70 75 80
Leu Thr Thr Leu Pro Ala Ser Ile Ala Asn Leu Ile Asn Leu Arg Glu
85 90 95
Leu Asp Val Ser Lys Asn Gly Ile Gln Glu Phe Pro Glu Asn Ile Lys
100 105 110
Asn Cys Lys Val Leu Thr Ile Val Glu Ala Ser Val Asn Pro Ile Ser
115 120 125
Lys Leu Pro Asp Gly Phe Ser Gln Leu Leu Asn Leu Thr Gln Leu Tyr
130 135 140
Leu Asn Asp Ala Phe Leu Glu Phe Leu Pro Ala Asn Phe Gly Arg Leu
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Thr Lys Leu Gln Ile Leu Glu Leu Arg Glu Asn Gln Leu Lys Met Leu
165 170 175
Pro Lys Thr Met Asn Arg Leu Thr Gln Leu Glu Arg Leu Asp Leu Gly
180 185 190
Ser Asn Glu Phe Thr Glu Val Pro Glu Val Leu Glu Gln Leu Ser Gly
195 200 205
Leu Lys Glu Phe Trp Met Asp Ala Asn Arg Leu Thr Phe Ile Pro Gly
210 215 220
Phe Ile Gly Ser Leu Lys Gln Leu Thr Tyr Leu Asp Val Ser Lys Asn
225 230 235 240
Asn Ile Glu Met Val Glu Glu Gly Ile Ser Thr Cys Glu Asn Leu Gln
245 250 255
Asp Leu Leu Ser Ser Asn Ser Leu Gln Gln Leu Pro Glu Thr Ile
260 265 270
Gly Ser Leu Lys Asn Ile Thr Thr Leu Lys Ile Asp Glu Asn Gln Leu
275 280 285
Met Tyr Leu Pro Asp Ser Ile Gly Gly Leu Ile Ser Val Glu Glu Leu
290 295 300
Asp Cys Ser Phe Asn Glu Val Glu Ala Leu Pro Ser Ser Ile Gly Gln
305 310 315 320

249

Leu Thr Asn Leu Arg Thr Phe Ala Ala Asp His Asn Tyr Leu Gln Gln
325 330 335
Leu Pro Pro Glu Ile Gly Ser Trp Lys Asn Ile Thr Val Leu Phe Leu
340 345 350
His Ser Asn Lys Leu Glu Thr Leu Pro Glu Glu Met Gly Asp Met Gln
355 360 365
Lys Leu Lys Val Ile Asn Leu Ser Asp Asn Arg Leu Lys Asn Leu Pro
370 375 380
Phe Ser Phe Thr Lys Leu Gln Gln Leu Thr Ala Met Trp Leu Ser Asp
385 390 395 400
Asn Gln Ser Lys Pro Leu Ile Pro Leu Gln Lys Glu Thr Asp Ser Glu
405 410 415
Thr Gln Lys Met Val Leu Thr Asn Tyr Met Phe Pro Gln Gln Pro Arg
420 425 430
Thr Glu Asp Val Met Phe Ile Ser Asp Asn Glu Ser Phe Asn Pro Ser
435 440 445
Leu Trp Glu Glu Gln Arg Lys Gln Arg Ala Gln Val Ala Phe Glu Cys
450 455 460
Asp Glu Asp Lys Asp Glu Arg Glu Ala Pro Pro Arg Glu Gly Asn Leu
465 470 475 480
Lys Arg Tyr Pro Thr Pro Tyr Pro Asp Glu Leu Lys Asn Met Val Lys
485 490 495
Thr Val Gln Thr Ile Val His Arg Leu Lys Asp Glu Glu Thr Asn Glu
500 505 510
Asp Ser Gly Arg Asp Leu Lys Pro His Glu Asp Gln Gln Asp Ile Asn
515 520 525
Lys Asp Val Gly Val Lys Thr Ser Glu Ser Thr Thr Val Lys Ser
530 535 540
Lys Val Asp Glu Arg Glu Lys Tyr Met Ile Gly Asn Ser Val Gln Lys
545 550 555 560
Ile Ser Glu Pro Glu Ala Glu Ile Ser Pro Gly Ser Leu Pro Val Thr
565 570 575
Ala Asn Met Lys Ala Ser Glu Asn Leu Lys His Ile Val Asn His Asp
580 585 590
Asp Val Phe Glu Glu Ser Glu Glu Leu Ser Ser Asp Glu Glu Met Lys
595 600 605
Met Ala Glu Met Arg Pro Pro Leu Ile Glu Thr Ser Ile Asn Gln Pro
610 615 620
Lys Val Val Ala Leu Ser Asn Asn Lys Lys Asp Asp Thr Lys Glu Thr
625 630 635 640
Asp Ser Leu Ser Asp Glu Val Thr His Asn Ser Asn Gln Asn Ser
645 650 655 660

250

645 650 655
 Asn Cys Ser Ser Pro Ser Arg Met Ser Asp Ser Val Ser Leu Asn Thr 670
 660 665
 Asp Ser Ser Gln Asp Thr Ser Leu Cys Ser Pro Val Lys Gln Thr His 685
 675 680
 Ile Asp Ile Asn Ser Lys Ile Arg Gln Glu Asp Glu Asn Phe Asn Ser 700
 690 695
 Leu Leu Gln Asn Gly Asp Ile Leu Asn Ser Ser Thr Glu Glu Lys Phe 720
 705 710 715
 Lys Ala His Asp Lys Lys Asp Phe Asn Leu Pro Glu Tyr Asp Leu Asn 735
 725 730
 Val Glu Glu Arg Leu Val Leu Ile Glu Lys Ser Val Asp Ser Thr Ala 750
 740 745
 Thr Ala Asp Asp Thr His Lys Leu Asp His Ile Asn Met Asn Leu Asn 765
 755 760
 Lys Leu Ile Thr Asn Asp Thr Phe Gln Pro Glu Ile Met Glu Arg Ser 780
 770 775
 Lys Thr Gln Asp Ile Val Leu Gly Thr Ser Phe Leu Ser Ile Asn Ser 800
 785 790 795
 Lys Glu Glu Thr Glu His Leu Glu Asn Gly Asn Lys Tyr Pro Asn Leu 815
 805 810
 Glu Ser Val Asn Lys Val Asn Gly His Ser Glu Glu Thr Ser Gln Ser 830
 820 825
 Pro Asn Arg Thr Glu Pro His Asp Ser Asp Cys Ser Val Asp Leu Gly 845
 835 840
 Ile Ser Lys Ser Thr Glu Asp Leu Ser Pro Gln Lys Ser Gly Pro Val 860
 850 855
 Gly Ser Val Val Lys Ser His Ser Ile Thr Asn Met Glu Ile Gly Gly 880
 865 870 875
 Leu Lys Ile Tyr Asp Ile Leu Ser Asp Asn Gly Pro Gln Gln Pro Ser 895
 885 890
 Thr Thr Val Lys Ile Thr Ser Ala Val Asp Gly Lys Asn Ile Val Arg 910
 900 905
 Ser Lys Ser Ala Thr Leu Leu Tyr Asp Gln Pro Leu Gln Val Phe Thr 925
 915 920
 Gly Ser Ser Ser Ser Asp Leu Ile Ser Gly Thr Lys Ala Ile Phe 940
 930 935
 Lys Phe Asp Ser Asn His Asn Pro Glu Glu Pro Asn Ile Ile Arg Gly 960
 945 950 955
 Pro Thr Ser Gly Pro Gln Ser Ala Pro Gln Ile Tyr Gly Pro Pro Gln 975
 965 970

Tyr Asn Ile Gln Tyr Ser Ser Ala Ala Val Lys Asp Thr Leu Trp 980
 985
 His Ser Lys Gln Asn Pro Gln Ile Asp His Ala Ser Phe Pro Pro Gln 1005
 995 1000
 Leu Leu Pro Arg Ser Glu Ser Thr Glu Asn Gln Ser Tyr Ala Lys 1020
 1010 1015
 His Ser Ala Asn Met Asn Phe Ser Asn His Asn Asn Val Arg Ala 1035
 1025 1030
 Asn Thr Ala Tyr His Leu His Gln Arg Leu Gly Pro Ala Arg His 1050
 1040 1045
 Gly Glu Met Trp Ala Ile Ser Pro Asn Asp Arg Leu Ile Pro Ala 1065
 1055 1060
 Val Thr Arg Ser Thr Ile Gln Arg Gln Ser Ser Val Ser Ser Thr 1080
 1070 1075
 Ala Ser Val Asn Leu Gly Asp Pro Gly Ser Thr Arg Arg Ala Gln 1095
 1085 1090
 Ile Pro Glu Gly Asp Tyr Leu Ser Tyr Arg Glu Phe His Ser Ala 1110
 1100 1105
 Gly Arg Thr Pro Pro Met Met Pro Gly Ser Gln Arg Pro Leu Ser 1125
 1115 1120
 Ala Arg Thr Tyr Ser Ile Asp Gly Pro Asn Ala Ser Arg Pro Gln 1140
 1130 1135
 Ser Ala Arg Pro Ser Ile Asn Glu Ile Pro Glu Arg Thr Met Ser 1155
 1145 1150
 Val Ser Asp Phe Asn Tyr Ser Arg Thr Ser Pro Ser Lys Arg Pro 1170
 1160 1165
 Asn Ala Arg Val Gly Ser Glu His Ser Leu Leu Asp Pro Pro Gly 1185
 1175 1180
 Lys Ser Lys Val Pro Arg Asp Trp Arg Glu Gln Val Leu Arg His 1200
 1190 1195
 Ile Glu Ala Lys Lys Leu Glu Lys Met Pro Leu Ser Asn Gly Gln 1215
 1205 1210
 Met Gly Gln Pro Leu Arg Pro Gln Ala Asn Tyr Ser Gln Ile His 1230
 1220 1225
 His Pro Pro Gln Ala Ser Val Ala Arg His Pro Ser Arg Glu Gln 1245
 1235 1240
 Leu Ile Asp Tyr Leu Met Leu Lys Val Ala His Gln Pro Pro Tyr 1260
 1250 1255
 Thr Gln Pro His Cys Ser Pro Arg Gln Gly His Glu Leu Ala Lys 1275
 1265 1270
 Gln Glu Ile Arg Val Arg Val Glu Lys Asp Pro Glu Leu Gly Phe 1290
 1280 1285

Ser Ile Ser Gly Gly Val Gly Gly Arg Gly Asn Pro Phe Arg Pro
1295 1300 1305
Asp Asp Asp Gly Ile Phe Val Thr Arg Val Gln Pro Glu Gly Pro
1310 1315 1320
Ala Ser Lys Leu Leu Gln Pro Gly Asp Lys Ile Ile Gln Ala Asn
1325 1330 1335
Gly Tyr Ser Phe Ile Asn Ile Glu His Gly Gln Ala Val Ser Leu
1340 1345 1350
Leu Lys Thr Phe Gln Asn Thr Val Glu Leu Ile Ile Val Arg Glu
1355 1360 1365
Val Ser Ser
1370
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<213> Homo sapiens
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20 25 30
Gly Phe Ser Gln Leu Leu Asn Leu Thr Gln Leu Tyr Leu Asn Asp Ala
35 40 45
Phe Leu Glu Phe Leu Pro Ala Asn Phe Gly Arg Leu Thr Lys Leu Gln
50 55 60
Ile Leu Glu Leu Arg Glu Asn Gln Leu Lys Met Leu Pro Lys Thr Met
65 70 75 80
Asn Arg Leu Thr Gln Leu Glu Arg Leu Asp Leu Gly Ser Asn Glu Phe
85 90 95
Thr Glu Val Pro Glu Val Leu Glu Gln Leu Ser Gly Leu Lys Glu Phe
100 105 110
Trp Met Asp Ala Asn Arg Leu Thr Phe Ile Pro Gly Phe Ile Gly Ser
115 120 125
Leu Lys Gln Leu Thr Tyr Leu Asp Val Ser Lys Asn Asn Ile Glu Met
130 135 140
Val Glu Glu Gly Ile Ser Thr Cys Glu Asn Leu Gln Asp Leu Leu Leu
145 150 155 160
Ser Ser Asn Ser Leu Gln Gln Leu Pro Glu Thr Ile Gly Ser Leu Lys
165 170 175
Asn Ile Thr Thr Leu Lys Ile Asp Glu Asn Gln Leu Met Tyr Leu Pro
180 185 190
Asp Ser Ile Gly Gly Leu Ile Ser Val Glu Glu Leu Asp Cys Ser Phe

195 200 205
Asn Glu Val Glu Ala Leu Pro Ser Ser Ile Gly Gln Leu Thr Asn Leu
210 215 220
Arg Thr Phe Ala Ala Asp His Asn Tyr Leu Gln Gln Leu Pro Pro Glu
225 230 235 240
Ile Gly Ser Trp Lys Asn Ile Thr Val Leu Phe Leu His Ser Asn Lys
245 250 255
Leu Glu Thr Leu Pro Glu Glu Met Gly Asp Met Gln Lys Leu Lys Val
260 265 270
Ile Asn Leu Ser Asp Asn Arg Leu Lys Asn Leu Pro Phe Ser Phe Thr
275 280 285
Lys Leu Gln Gln Leu Thr Ala Met Trp Leu Ser Asp Asn Gln Ser Lys
290 295 300
Pro Leu Ile Pro Leu Gln Lys Glu Thr Asp Ser Glu Thr Gln Lys Met
305 310 315 320
Val Leu Thr Asn Tyr Met Phe Pro Gln Gln Pro Arg Thr Glu Asp Val
325 330 335
Met Phe Ile Ser Asp Asn Glu Ser Phe Asn Pro Ser Leu Trp Glu Glu
340 345 350
Gln Arg Lys Gln Arg Ala Gln Val Ala Phe Glu Cys Asp Glu Asp Lys
355 360 365
Asp Glu Arg Glu Ala Pro Pro Arg Glu Gly Asn Leu Lys Arg Tyr Pro
370 375 380
Thr Pro Tyr Pro Asp Glu Leu Lys Asn Met Val Lys Thr Val Gln Thr
385 390 395 400
Ile Val His Arg Leu Lys Asp Glu Glu Thr Asn Glu Asp Ser Gly Arg
405 410 415
Asp Leu Lys Pro His Glu Asp Gln Asp Ile Asn Lys Asp Val Gly
420 425 430
Val Lys Thr Ser Glu Ser Thr Thr Thr Val Lys Ser Lys Val Asp Glu
435 440 445
Arg Glu Lys Tyr Met Ile Gly Asn Ser Val Gln Lys Ile Ser Glu Pro
450 455 460
Glu Ala Glu Ile Ser Pro Gly Ser Leu Pro Val Thr Ala Asn Met Lys
465 470 475 480
Ala Ser Glu Asn Leu Lys His Ile Val Asn His Asp Asp Val Phe Glu
485 490 495
Glu Ser Glu Glu Leu Ser Ser Asp Glu Glu Met Lys Met Ala Glu Met
500 505 510
Arg Pro Pro Leu Ile Glu Thr Ser Ile Asn Gln Pro Lys Val Val Ala
515 520 525

Leu Ser Asn Asn Lys Lys Asp Asp Thr Lys Glu Thr Asp Ser Leu Ser
 530 535 540
 Asp Glu Val Thr His Asn Ser Asn Gln Asn Asn Ser Asn Cys Ser Ser
 545 550 555 560
 Pro Ser Arg Met Ser Asp Ser Val Ser Leu Asn Thr Asp Ser Ser Gln
 565 570 575
 Asp Thr Ser Leu Cys Ser Pro Val Lys Gln Thr His Ile Asp Ile Asn
 580 585 590
 Ser Lys Ile Arg Gln Glu Asp Glu Asn Phe Asn Ser Leu Leu Gln Asn
 595 600 605
 Gly Asp Ile Leu Asn Ser Ser Thr Glu Glu Lys Phe Lys Ala His Asp
 610 615 620
 Lys Lys Asp Phe Asn Leu Pro Glu Tyr Asp Leu Asn Val Glu Glu Arg
 625 630 635 640
 Leu Val Leu Ile Glu Lys Ser Val Asp Ser Thr Ala Thr Ala Asp Asp
 645 650 655
 Thr His Lys Leu Asp His Ile Asn Met Asn Leu Asn Lys Leu Ile Thr
 660 665 670
 Asn Asp Thr Phe Gln Pro Glu Ile Met Glu Arg Ser Lys Thr Gln Asp
 675 680 685
 Ile Val Leu Gly Thr Ser Phe Leu Ser Ile Asn Ser Lys Glu Glu Thr
 690 695 700
 Glu His Leu Glu Asn Gly Asn Lys Tyr Pro Asn Leu Glu Ser Val Asn
 705 710 715 720
 Lys Val Asn Gly His Ser Glu Glu Thr Ser Gln Ser Pro Asn Arg Thr
 725 730 735
 Glu Pro His Asp Ser Asp Cys Ser Val Asp Leu Glu Ile Ser Lys Ser
 740 745 750
 Thr Glu Asp Leu Ser Pro Gln Lys Ser Gly Pro Val Gly Ser Val Val
 755 760 765
 Lys Ser His Ser Ile Thr Asn Met Glu Ile Gly Gly Leu Lys Ile Tyr
 770 775 780
 Asp Ile Leu Ser Asp Asn Gly Pro Gln Gln Pro Ser Thr Thr Val Lys
 785 790 795 800
 Ile Thr Ser Ala Val Asp Gly Lys Asn Ile Val Arg Ser Lys Ser Ala
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 Thr Leu Leu Tyr Asp Gln Pro Leu Gln Val Phe Thr Gly Ser Ser Ser
 820 825 830
 Ser Ser Asp Leu Ile Ser Gly Thr Lys Ala Ile Phe Lys Phe Asp Ser
 835 840 845
 Asn His Asn Pro Glu Glu Pro Asn Ile Ile Arg Gly Pro Thr Ser Gly
 850 855 860

Pro Gln Ser Ala Pro Gln Ile Tyr Gly Pro Pro Gln Tyr Asn Ile Gln
 865 870 875 880
 Tyr Ser Ser Ser Ala Ala Val Lys Asp Thr Leu Trp His Ser Lys Gln
 885 890 895
 Asn Pro Gln Ile Asp His Ala Ser Phe Pro Pro Gln Leu Leu Pro Arg
 900 905 910
 Ser Glu Ser Thr Glu Asn Gln Ser Tyr Ala Lys His Ser Ala Asn Met
 915 920 925
 Asn Phe Ser Asn His Asn Asn Val Arg Ala Asn Thr Ala Tyr His Leu
 930 935 940
 His Gln Arg Leu Gly Pro Ala Arg His Gly Glu Met Trp Ala Ile Ser
 945 950 955 960
 Pro Asn Asp Arg Leu Ile Pro Ala Val Thr Arg Ser Thr Ile Gln Arg
 965 970 975
 Gln Ser Ser Val Ser Ser Thr Ala Ser Val Asn Leu Gly Asp Pro Gly
 980 985 990
 Ser Thr Arg Arg Ala Gln Ile Pro Glu Gly Asp Tyr Leu Ser Tyr Arg
 995 1000 1005
 Glu Phe His Ser Ala Gly Arg Thr Pro Pro Met Met Pro Gly Ser
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 Ala Ser Arg Pro Gln Ser Ala Arg Pro Ser Ile Asn Glu Ile Pro
 1040 1045 1050
 Glu Arg Thr Met Ser Val Ser Asp Phe Asn Tyr Ser Arg Thr Ser
 1055 1060 1065
 Pro Ser Lys Arg Pro Asn Ala Arg Val Gly Ser Glu His Ser Leu
 1070 1075 1080
 Leu Asp Pro Pro Gly Lys Ser Lys Val Pro Arg Asp Trp Arg Glu
 1085 1090 1095
 Gln Val Leu Arg His Ile Glu Ala Lys Lys Leu Glu Lys Met Pro
 1100 1105 1110
 Leu Ser Asn Gly Gln Met Gly Gln Pro Leu Arg Pro Gln Ala Asn
 1115 1120 1125
 Tyr Ser Gln Ile His His Pro Pro Gln Ala Ser Val Ala Arg His
 1130 1135 1140
 Pro Ser Arg Glu Gln Leu Ile Asp Tyr Leu Met Leu Lys Val Ala
 1145 1150 1155
 His Gln Pro Pro Tyr Thr Gln Pro His Cys Ser Pro Arg Gln Gly
 1160 1165 1170
 His Glu Leu Ala Lys Gln Glu Ile Arg Val Arg Val Glu Lys Asp

1175 1180 1185
 Pro Glu Leu Gly Phe Ser Ile Ser Gly Gly Val Gly Gly Arg Gly
 1190 1195 1200
 Asn Pro Phe Arg Pro Asp Asp Gly Ile Phe Val Thr Arg Val
 1205 1210 1215
 Gln Pro Glu Gly Pro Ala Ser Lys Leu Leu Gln Pro Gly Asp Lys
 1220 1225 1230
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 35 40 45
 Asn Leu Glu Thr Tyr Trp Gln Ser Asp Gly Ser Gln Pro His Leu Val
 50 55 60
 Asn Ile Gln Phe Arg Arg Lys Thr Thr Val Lys Thr Leu Cys Ile Tyr
 65 70 75 80
 Ala Asp Tyr Lys Ser Asp Glu Ser Tyr Thr Pro Ser Lys Ile Ser Val
 85 90 95
 Arg Val Gly Asn Asn Phe His Asn Leu Leu Gln Glu Ile Arg Gln Leu Glu
 100 105 110
 Leu Val Glu Pro Ser Gly Trp Ile His Val Pro Leu Thr Asp Asn His
 115 120 125
 Lys Lys Pro Thr Arg Thr Phe Met Ile Gln Ile Ala Val Leu Ala Asn
 130 135 140
 His Gln Asn Gly Arg Asp Thr His Met Arg Gln Ile Lys Ile Tyr Thr
 145 150 155 160
 Pro Val Glu Glu Ser Ser Ile Gly Lys Phe Pro Arg Cys Thr Thr Ile
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 Asp Phe Met Tyr Tyr Arg Ser Ile Arg
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257

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 Ser Ser Val Lys Met Val His Gly Asn Ile Thr Pro Glu Asn Ile Ile
 35 40 45
 Leu Asn Lys Ser Gly Ala Trp Lys Ile Met Gly Phe Asp Phe Cys Val
 50 55 60
 Ser Ser Thr Asn Pro Ser Glu Gln Glu Pro Lys Phe Pro Cys Lys Glu
 65 70 75 80
 Trp Asp Pro Asn Leu Pro Ser Leu Cys Leu Pro Asn Pro Glu Tyr Leu
 85 90 95
 Ala Pro Glu Tyr Ile Leu Ser Val Ser Cys Glu Thr Ala Ser Asp Met
 100 105 110
 Tyr Ser Leu Gly Thr Val Met Tyr Ala Val Phe Asn Lys Gly Lys Pro
 115 120 125
 Ile Phe Glu Val Asn Lys Gln Asp Ile Tyr Lys Ser Phe Ser Arg Gln
 130 135 140
 Leu Asp Gln Leu Ser Arg Leu Gly Ser Ser Ser Leu Thr Asn Ile Pro
 145 150 155 160
 Glu Glu Val Arg Glu His Val Lys Leu Leu Asn Val Thr Pro Thr
 165 170 175
 Val Arg Pro Asp Ala Asp Gln Met Thr Lys Ile Pro Phe Phe Asp Asp
 180 185 190
 Val Gly Ala Val Thr Leu Gln Tyr Phe Asp Thr Leu Phe Gln Arg Asp
 195 200 205
 Asn Leu Gln Lys Ser Gln Phe Phe Lys Gly Leu Pro Lys Val Leu Pro
 210 215 220
 Lys Leu Pro Lys Arg Val Ile Val Gln Arg Ile Leu Pro Cys Leu Thr
 225 230 235 240
 Ser Glu Phe Val Asn Pro Asp Met Val Pro Phe Val Leu Pro Asn Val
 245 250 255
 Leu Leu Ile Ala Glu Glu Cys Thr Lys Glu Glu Tyr Val Lys Leu Ile
 260 265 270
 Leu Pro Glu Leu Gly Pro Val Phe Lys Gln Gln Glu Pro Ile Gln Ala
 275 280 285
 Ser Asn Met Ile Leu Leu Ile Phe Leu Gln Lys Met Asp Leu Leu
 290 295 300

258

Thr Lys Thr Pro Pro Asp Glu Ile Lys Asn Ser Val Leu Pro Met Val
 305 310 315 320
 Tyr Arg Ala Leu Glu Ala Pro Ser Ile Gln Ile Gln Glu Leu Cys Leu
 325 330 335
 Asn Ile Ile Pro Thr Phe Ala Asn Leu Ile Asp Tyr Pro Ser Met Lys
 340 345 350
 Asn Ala Leu Ile Pro Arg Ile Lys Asn Ala Cys Leu Gln Thr Ser Ser
 355 360 365
 Leu Ala Val Arg Val Asn Ser Leu Val Cys Leu Gly Lys Ile Leu Glu
 370 375 380
 Tyr Leu Asp Lys Trp Phe Val Leu Asp Asp Ile Leu Pro Phe Leu Gln
 385 390 395 400
 Gln Ile Pro Ser Lys Glu Pro Ala Val Leu Met Gly Ile Leu Gly Ile
 405 410 415
 Tyr Lys Cys Thr Phe Thr His Lys Lys Leu Gly Ile Thr Lys Glu Gln
 420 425 430
 Leu Ala Gly Lys Val Leu Pro His Leu Ile Pro Leu Ser Ile Glu Asn
 435 440 445
 Asn Leu Asn Leu Asn Gln Phe Asn Ser Phe Ile Ser Val Ile Lys Glu
 450 455 460
 Met Leu Asn Arg Leu Glu Ser Glu His Lys Thr Lys Leu Glu Gln Leu
 465 470 475 480
 His Ile Met Gln Glu Gln Gln Lys Ser Leu Asp Ile Gly Asn Gln Met
 485 490 495
 Asn Val Ser Glu Glu Met Lys Val Thr Asn Ile Gly Asn Gln Gln Ile
 500 505 510
 Asp Lys Val Phe Asn Asn Ile Gly Ala Asp Leu Leu Thr Gly Ser Glu
 515 520 525
 Ser Glu Asn Lys Glu Asp Gly Leu Gln Asn Lys His Lys Arg Ala Ser
 530 535 540
 Leu Thr Leu Glu Glu Lys Gln Lys Leu Ala Lys Glu Gln Gln Ala
 545 550 555 560
 Gln Lys Leu Lys Ser Gln Gln Pro Leu Lys Pro Gln Val His Thr Pro
 565 570 575
 Val Ala Thr Val Lys Gln Thr Lys Asp Leu Thr Asp Thr Leu Met Asp
 580 585 590
 Asn Met Ser Ser Leu Thr Ser Leu Ser Val Ser Thr Pro Lys Ser Ser
 595 600 605
 Ala Ser Ser Thr Phe Thr Ser Val Pro Ser Met Gly Ile Gly Met Met
 610 615 620
 Phe Ser Thr Pro Thr Asp Asn Thr Lys Arg Asn Leu Thr Asn Gly Leu

625 630 635 640
 Asn Ala Asn Met Gly Phe Gln Thr Ser Gly Phe Asn Met Pro Val Asn
 645 650 655
 Thr Asn Gln Asn Phe Tyr Ser Ser Pro Ser Thr Val Gly Val Thr Lys
 660 665 670
 Met Thr Leu Gly Thr Pro Thr Leu Pro Asn Phe Asn Ala Leu Ser
 675 680 685
 Val Pro Pro Ala Gly Ala Lys Gln Thr Gln Gln Arg Pro Thr Asp Met
 690 695 700
 Ser Ala Leu Asn Asn Leu Phe Gly Pro Gln Lys Pro Lys Val Ser Met
 705 710 715 720
 Asn Gln Leu Ser Gln Gln Lys Pro Asn Gln Trp Leu Asn Gln Phe Val
 725 730 735
 Pro Pro Gln Gly Ser Pro Thr Met Gly Ser Ser Val Met Gly Thr Gln
 740 745 750
 Met Asn Val Ile Gly Gln Ser Ala Phe Gly Met Gln Gly Asn Pro Phe
 755 760 765
 Phe Asn Pro Gln Asn Phe Ala Gln Pro Thr Thr Met Thr Asn Ser
 770 775 780
 Ser Ser Ala Ser Asn Asp Leu Lys Asp Leu Phe Gly
 785 790 795
 <210> 127
 <211> 735
 <212> PRT
 <213> Homo sapiens
 <400> 127
 Met Gly Phe Asp Phe Cys Val Ser Ser Thr Asn Pro Ser Glu Gln Glu
 1 5 10 15
 Pro Lys Phe Pro Cys Lys Glu Trp Asp Pro Asn Leu Pro Ser Leu Cys
 20 25 30
 Leu Pro Asn Pro Glu Tyr Leu Ala Pro Glu Tyr Ile Leu Ser Val Ser
 35 40 45
 Cys Glu Thr Ala Ser Asp Met Tyr Ser Leu Gly Thr Val Met Tyr Ala
 50 55 60
 Val Phe Asn Lys Gly Lys Pro Ile Phe Glu Val Asn Lys Gln Asp Ile
 65 70 75 80
 Tyr Lys Ser Phe Ser Arg Gln Leu Asp Gln Leu Ser Arg Leu Gly Ser
 85 90 95
 Ser Ser Leu Thr Asn Ile Pro Glu Glu Val Arg Glu His Val Lys Leu
 100 105 110
 Leu Leu Asn Val Thr Pro Thr Val Arg Pro Asp Ala Asp Gln Met Thr
 115 120 125

Lys Ile Pro Phe Asp Val Gly Ala Val Thr Leu Gln Tyr Phe 130 135 140
 Asp Thr Leu Phe Gln Arg Asp Asn Leu Gln Lys Ser Gln Phe Lys 145 150 155 160
 Gly Leu Leu Lys Val Leu Pro Lys Leu Pro Lys Arg Val Ile Val Gln 165 170 175
 Arg Ile Leu Pro Cys Leu Thr Ser Glu Phe Val Asn Pro Asp Met Val 180 185 190
 Pro Phe Val Leu Pro Asn Val Leu Leu Ile Ala Glu Gly Cys Thr Lys 195 200 205
 Glu Gly Tyr Val Lys Leu Ile Leu Pro Glu Leu Gly Pro Val Phe Lys 210 215 220
 Gln Gln Glu Pro Ile Gln Ile Leu Leu Ile Phe Leu Gln Lys Met Asp 225 230 235 240
 Leu Leu Leu Thr Arg Thr Pro Pro Asp Glu Ile Lys Asn Ser Val Leu 245 250 255
 Pro Met Val Tyr Arg Ala Leu Glu Ala Pro Ser Ile Gln Ile Gln Glu 260 265 270
 Leu Cys Leu Asn Ile Ile Pro Thr Phe Ala Asn Leu Ile Asp Tyr Pro 275 280 285
 Ser Met Lys Asn Ala Leu Ile Pro Arg Ile Lys Asn Ala Cys Leu Gln 290 295 300
 Thr Ser Ser Leu Ala Val Arg Val Asn Ser Leu Val Cys Leu Gly Lys 305 310 315 320
 Ile Leu Glu Tyr Leu Asp Lys Trp Phe Val Leu Asp Asp Ile Leu Pro 325 330 335
 Phe Leu Gln Gln Ile Pro Ser Lys Glu Pro Ala Val Leu Met Gly Ile 340 345 350
 Leu Gly Ile Tyr Lys Cys Thr Phe Thr His Lys Lys Leu Gly Ile Thr 355 360 365
 Lys Glu Gln Leu Ala Gly Lys Val Leu Pro His Leu Ile Pro Leu Ser 370 375 380
 Ile Glu Asn Asn Leu Asn Leu Asn Gln Phe Asn Ser Phe Ile Ser Val 385 390 395 400
 Ile Lys Glu Met Leu Asn Arg Leu Glu Ser Glu His Lys Thr Lys Leu 405 410 415
 Glu Gln Leu His Ile Met Gln Glu Gln Gln Lys Ser Leu Asp Ile Gly 420 425 430
 Asn Arg Met Asn Val Ser Glu Glu Met Lys Val Thr Asn Ile Gly Asn 435 440 445
 Gln Gln Ile Asp Lys Val Phe Asn Asn Ile Gly Ala Asp Leu Thr 450 455 460

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Gly Ser Glu Ser Glu Asn Lys Glu Asp Gly Leu Gln Asn Lys His Lys 465 470 475 480
 Arg Ala Ser Leu Thr Leu Glu Glu Lys Gln Lys Leu Ala Lys Glu Gln 485 490 495
 Glu Gln Ala Gln Lys Leu Lys Ser Gln Gln Pro Leu Lys Pro Gln Val 500 505 510
 His Thr Pro Val Ala Thr Val Lys Gln Thr Lys Asp Leu Thr Asp Thr 515 520 525
 Leu Met Asp Asn Met Ser Ser Leu Thr Ser Leu Ser Val Ser Thr Pro 530 535 540
 Lys Ser Ser Ala Ser Ser Thr Phe Thr Ser Val Pro Ser Met Gly Ile 545 550 555 560
 Gly Met Met Phe Ser Thr Pro Thr Asp Asn Thr Lys Arg Asn Leu Thr 565 570 575
 Asn Gly Leu Asn Ala Asn Met Gly Phe Gln Thr Ser Gly Phe Asn Met 580 585 590
 Pro Val Asn Thr Asn Gln Asn Phe Tyr Ser Ser Pro Ser Thr Val Gly 595 600 605
 Val Thr Lys Met Thr Leu Gly Thr Pro Thr Leu Pro Asn Phe Asn 610 615 620
 Ala Leu Ser Val Pro Pro Ala Gly Ala Lys Gln Thr Gln Gln Arg Pro 625 630 635 640
 Thr Asp Met Ser Ala Leu Asn Asn Leu Phe Gly Pro Gln Lys Pro Lys 645 650 655
 Val Ser Met Asn Gln Leu Ser Gln Lys Pro Asn Gln Trp Leu Asn 660 665 670
 Gln Phe Val Pro Pro Gln Gly Ser Pro Thr Met Gly Ser Ser Val Met 675 680 685
 Gly Thr Gln Met Asn Val Ile Gly Gln Ser Ala Phe Gly Met Gln Gly 690 695 700
 Asn Pro Phe Phe Asn Pro Gln Asn Phe Ala Gln Pro Pro Thr Thr Met 705 710 715 720
 Thr Asn Ser Ser Ser Ala Ser Asn Asp Leu Lys Asp Leu Phe Gly 725 730 735
 <210> 128
 <211> 470
 <212> PRT
 <213> Homo sapiens
 <400> 128
 Met Pro Gly Phe Asp Tyr Lys Phe Leu Glu Lys Pro Lys Arg Arg Leu 1 5 10 15
 Leu Cys Pro Leu Cys Gly Lys Pro Met Arg Glu Pro Val Gln Val Ser

262

20 25 30
 Thr Cys Gly His Arg Phe Cys Asp Thr Cys Leu Gln Glu Phe Leu Ser 45
 35
 Glu Gly Val Phe Lys Cys Pro Glu Asp Gln Leu Pro Leu Asp Tyr Ala 60
 50 55
 Lys Ile Tyr Pro Asp Pro Glu Leu Glu Val Gln Val Leu Gly Leu Pro 80
 65 70 75
 Ile Arg Cys Ile His Ser Glu Glu Gly Cys Arg Trp Ser Gly Pro Leu 95
 85 90
 Arg His Leu Gln Gly His Leu Asn Thr Cys Ser Phe Asn Val Ile Pro 110
 100 105
 Cys Pro Asn Arg Cys Pro Met Lys Leu Ser Arg Arg Asp Leu Pro Ala 125
 115 120
 His Leu Gln His Asp Cys Pro Lys Arg Arg Leu Lys Cys Glu Phe Cys 140
 130 135
 Gly Cys Asp Phe Ser Gly Glu Ala Tyr Glu Ser His Glu Gly Met Cys 160
 145 150 155
 Pro Gln Glu Ser Val Tyr Cys Glu Asn Lys Cys Gly Ala Arg Met Met 175
 165 170
 Arg Gly Leu Leu Ala Gln His Ala Thr Ser Glu Cys Pro Lys Arg Thr 190
 180 185
 Gln Pro Cys Thr Tyr Cys Thr Lys Glu Phe Val Phe Asp Thr Ile Gln 205
 195 200
 Ser His Gln Tyr Gln Cys Pro Arg Leu Pro Val Ala Cys Pro Asn Gln 220
 210 215
 Cys Gly Val Gly Thr Val Ala Arg Glu Asp Leu Pro Gly His Leu Lys 240
 225 230 235
 Asp Ser Cys Asn Thr Ala Leu Val Leu Cys Pro Phe Lys Asp Ser Gly 255
 245 250
 Cys Lys His Arg Cys Pro Lys Leu Ala Met Ala Arg His Val Glu Glu 270
 260 265
 Ser Val Lys Pro His Leu Ala Met Met Cys Ala Leu Val Ser Arg Gln 285
 275 280
 Arg Gln Glu Leu Gln Glu Leu Arg Arg Glu Leu Glu Leu Ser Val 300
 290 295
 Gly Ser Asp Gly Val Leu Ile Trp Lys Ile Gly Ser Tyr Gly Arg Arg 320
 305 310 315
 Leu Gln Glu Ala Lys Ala Lys Pro Asn Leu Glu Cys Phe Ser Pro Ala 335
 325 330
 Phe Tyr Thr His Lys Tyr Gly Tyr Lys Leu Gln Val Ser Ala Phe Leu 350
 340 345

Asn Gly Asn Gly Ser Gly Glu Gly Thr His Leu Ser Leu Tyr Ile Arg 365
 370 375 380
 Val Leu Pro Gly Ala Phe Asp Asn Leu Leu Glu Trp Pro Phe Ala Arg 395
 385 390 395
 Arg Val Thr Phe Ser Leu Leu Asp Gln Ser Asp Pro Gly Leu Ala Lys 410
 405 415
 Pro Gln His Val Thr Glu Thr Phe His Pro Asp Pro Asn Trp Lys Asn 430
 420 425
 Phe Gln Lys Pro Gly Thr Trp Arg Gly Ser Leu Asp Glu Ser Ser Leu 445
 435 440
 Gly Phe Gly Tyr Pro Lys Phe Ile Ser His Gln Asp Ile Arg Lys Arg 460
 450 455
 Asn Tyr Val Arg Asp Ala Val Phe Ile Arg Ala Ala Val Glu Leu 470
 465 470
 Pro Arg Lys Ile Leu Ser
 <210> 129
 <211> 543
 <212> PRT
 <213> Homo sapiens
 <400> 129
 Met Glu Ser Ser Lys Lys Met Asp Ser Pro Gly Ala Leu Gln Thr Asn 15
 1 5 10
 Pro Pro Leu Lys Leu His Thr Asp Arg Ser Ala Gly Thr Pro Val Phe 30
 20 25
 Val Pro Glu Gln Gly Tyr Lys Glu Lys Phe Val Lys Thr Val Glu 45
 35 40
 Asp Lys Tyr Lys Cys Glu Lys Cys His Leu Val Leu Cys Ser Pro Lys 60
 50 55
 Gln Thr Glu Cys Gly His Arg Phe Cys Glu Ser Cys Met Ala Ala Leu 80
 65 70 75
 Leu Ser Ser Ser Pro Lys Cys Thr Ala Cys Gln Glu Ser Ile Val 95
 85 90
 Lys Asp Lys Val Phe Lys Asp Asn Cys Cys Lys Arg Glu Ile Leu Ala 110
 100 105
 Leu Gln Ile Tyr Cys Arg Asn Glu Ser Arg Gly Cys Ala Glu Gln Leu 125
 115 120
 Thr Leu Gly His Leu Leu Val His Leu Lys Asn Asp Cys His Phe Glu 140
 130 135
 Glu Leu Pro Cys Val Arg Pro Asp Cys Lys Glu Lys Val Leu Arg Lys 160
 145 150 155
 Asp Leu Arg Asp His Val Glu Lys Ala Cys Lys Tyr Arg Glu Ala Thr 175
 165 170

Cys Ser His Cys Lys Ser Gln Val Pro Met Ile Ala Leu Gln Lys His
 180 185 190
 Glu Asp Thr Asp Cys Pro Cys Val Val Ser Cys Pro His Lys Cys
 195 200 205
 Ser Val Gln Thr Leu Leu Arg Ser Glu Gly Thr Asn Gln Gln Ile Lys
 210 215 220
 Ala His Glu Ala Ser Ser Ala Val Gln His Val Asn Leu Lys Glu
 225 230 235 240
 Trp Ser Asn Ser Leu Glu Lys Lys Val Ser Leu Leu Gln Asn Glu Ser
 245 250 255
 Val Glu Lys Asn Lys Ser Ile Gln Ser Leu His Asn Gln Ile Cys Ser
 260 265 270
 Phe Glu Ile Glu Ile Glu Arg Gln Lys Glu Met Leu Arg Asn Asn Glu
 275 280 285
 Ser Lys Ile Leu His Leu Gln Arg Val Ile Asp Ser Gln Ala Glu Lys
 290 295 300
 Leu Lys Glu Leu Asp Lys Glu Ile Arg Ser Phe Arg Gln Asn Trp Glu
 305 310 315 320
 Glu Ala Asp Ser Met Lys Ser Ser Val Glu Ser Leu Gln Asn Arg Val
 325 330 335
 Thr Glu Leu Glu Ser Val Asp Lys Ser Ala Gly Gln Val Ala Arg Asn
 340 345 350
 Thr Gly Leu Leu Glu Ser Gln Leu Ser Arg His Asp Gln Met Leu Ser
 355 360 365
 Val His Asp Ile Arg Leu Ala Asp Met Asp Leu Arg Phe Gln Val Leu
 370 375 380
 Glu Thr Ala Ser Tyr Asn Gly Val Leu Ile Trp Lys Ile Arg Asp Tyr
 385 390 395 400
 Lys Arg Arg Lys Gln Glu Ala Val Met Gly Lys Thr Leu Ser Leu Tyr
 405 410 415
 Ser Gln Pro Phe Tyr Thr Gly Tyr Phe Gly Tyr Lys Met Cys Ala Arg
 420 425 430
 Val Tyr Leu Asn Gly Asp Gly Met Gly Lys Gly Thr His Leu Ser Leu
 435 440 445
 Phe Phe Val Ile Met Arg Gly Glu Tyr Asp Ala Leu Leu Pro Trp Pro
 450 455 460
 Phe Lys Gln Lys Val Thr Leu Met Leu Met Asp Gln Gly Ser Ser Arg
 465 470 475 480
 Arg His Leu Gly Asp Ala Phe Lys Pro Asp Pro Asn Ser Ser Ser Phe
 485 490 495
 Lys Lys Pro Thr Gly Glu Met Asn Ile Ala Ser Gly Cys Pro Val Phe

500 505 510
 Val Ala Gln Thr Val Leu Glu Asn Gly Thr Tyr Ile Lys Asp Asp Thr
 515 520 525
 Ile Phe Ile Lys Val Ile Val Asp Thr Ser Asp Leu Pro Asp Pro
 530 535 540
 <210> 130
 <211> 501
 <212> PRT
 <213> Homo sapiens
 <400> 130
 Met Ala Ala Ser Val Thr Pro Pro Gly Ser Leu Glu Leu Gln
 1 5 10 15
 Pro Gly Phe Ser Lys Thr Leu Leu Gly Thr Lys Leu Glu Ala Lys Tyr
 20 25 30
 Leu Cys Ser Ala Cys Arg Asn Val Leu Arg Arg Pro Phe Gln Ala Gln
 35 40 45
 Cys Gly His Arg Tyr Cys Ser Phe Cys Leu Ala Ser Ile Leu Ser Ser
 50 55 60
 Gly Pro Gln Asn Cys Ala Ala Cys Val His Glu Gly Ile Tyr Glu Glu
 65 70 75 80
 Gly Ile Ser Ile Leu Glu Ser Ser Ser Ala Phe Pro Asp Asn Ala Ala
 85 90 95
 Arg Arg Glu Val Glu Ser Leu Pro Ala Val Cys Pro Ser Asp Gly Cys
 100 105 110
 Thr Trp Lys Gly Thr Leu Lys Glu Tyr Glu Ser Cys His Glu Gly Arg
 115 120 125
 Cys Pro Leu Met Leu Thr Glu Cys Pro Ala Cys Lys Gly Leu Val Arg
 130 135 140
 Leu Gly Glu Lys Glu Arg His Leu Glu His Glu Cys Pro Glu Arg Ser
 145 150 155 160
 Leu Ser Cys Arg His Cys Arg Ala Pro Cys Cys Gly Ala Asp Val Lys
 165 170 175
 Ala His His Glu Val Cys Pro Lys Phe Pro Leu Thr Cys Asp Gly Cys
 180 185 190
 Gly Lys Lys Lys Ile Pro Arg Glu Lys Phe Gln Asp His Val Lys Thr
 195 200 205
 Cys Gly Lys Cys Arg Val Pro Cys Arg Phe His Ala Ile Gly Cys Leu
 210 215 220
 Glu Thr Val Glu Gly Glu Lys Gln Gln Glu His Glu Val Gln Trp Leu
 225 230 235 240
 Arg Glu His Leu Ala Met Leu Ser Ser Val Leu Glu Ala Lys Pro
 245 250 255

Leu Leu Gly Asp Gln Ser His Ala Gly Ser Glu Leu Leu Gln Arg Cys
 260 265 270
 Glu Ser Leu Glu Lys Lys Thr Ala Thr Phe Glu Asn Ile Val Cys Val
 275 280 285
 Leu Asn Arg Glu Val Glu Arg Val Ala Met Thr Ala Glu Ala Cys Ser
 290 295 300
 Arg Gln His Arg Leu Asp Gln Asp Lys Ile Glu Ala Leu Ser Ser Lys
 305 310 315 320
 Val Gln Gln Leu Glu Arg Ser Ile Gly Leu Lys Asp Leu Ala Met Ala
 325 330 335
 Asp Leu Glu Gln Lys Val Arg Pro Phe Gln Ala Gln Cys Gly His Arg
 340 345 350
 Tyr Cys Ser Phe Cys Leu Ala Ser Ile Leu Arg Lys Leu Gln Glu Ala
 355 360 365
 Val Ala Gly Arg Ile Pro Ala Ile Phe Ser Pro Ala Phe Tyr Thr Ser
 370 375 380
 Arg Tyr Gly Tyr Lys Met Cys Leu Arg Ile Tyr Leu Asn Gly Asp Gly
 385 390 395 400
 Thr Gly Arg Gly Thr His Leu Ser Leu Phe Phe Val Val Met Lys Gly
 405 410 415
 Pro Asn Asp Ala Leu Leu Arg Trp Pro Phe Asn Gln Lys Val Thr Leu
 420 425 430
 Met Leu Leu Asp Gln Asn Asn Arg Glu His Val Ile Asp Ala Phe Arg
 435 440 445
 Pro Asp Val Thr Ser Ser Ser Phe Gln Arg Pro Val Asn Asp Met Asn
 450 455 460
 Ile Ala Ser Gly Cys Pro Leu Phe Cys Pro Val Ser Lys Met Glu Ala
 465 470 475 480
 Lys Asn Ser Tyr Val Arg Asp Ala Ile Phe Ile Lys Ala Ile Val
 485 490 495
 Asp Leu Thr Gly Leu
 500
 <210> 131
 <211> 568
 <212> PRT
 <213> Homo sapiens
 <400> 131
 Met Glu Ser Ser Lys Lys Met Asp Ser Pro Gly Ala Leu Gln Thr Asn
 1 5 10 15
 Pro Pro Leu Lys Leu His Thr Asp Arg Ser Ala Gly Thr Pro Val Phe
 20 25 30
 Val Pro Glu Gln Gly Tyr Lys Glu Lys Phe Val Lys Thr Val Glu
 35 40 45

Asp Lys Tyr Lys Cys Glu Lys Cys His Leu Val Leu Cys Ser Pro Lys
 50 55 60
 Gln Thr Glu Cys Gly His Arg Phe Cys Glu Ser Cys Met Ala Ala Leu
 65 70 75 80
 Leu Ser Ser Ser Ser Pro Lys Cys Thr Ala Cys Gln Glu Ser Ile Val
 85 90 95
 Lys Asp Lys Val Phe Lys Asp Asn Cys Lys Arg Glu Ile Leu Ala
 100 105 110
 Leu Gln Ile Tyr Cys Arg Asn Glu Ser Arg Gly Cys Ala Glu Gln Leu
 115 120 125
 Met Leu Gly His Leu Leu Val His Leu Lys Asn Asp Cys His Phe Glu
 130 135 140
 Glu Leu Pro Cys Val Arg Pro Asp Cys Lys Glu Lys Val Leu Arg Lys
 145 150 155 160
 Asp Leu Arg Asp His Val Glu Lys Ala Cys Lys Tyr Arg Glu Ala Thr
 165 170 175
 Cys Ser His Cys Lys Ser Gln Val Pro Met Ile Ala Leu Gln Lys His
 180 185 190
 Glu Asp Thr Asp Cys Pro Cys Val Val Ser Cys Pro His Lys Cys
 195 200 205
 Ser Val Gln Thr Leu Leu Arg Ser Glu Leu Ser Ala His Leu Ser Glu
 210 215 220
 Cys Val Asn Ala Pro Ser Thr Cys Ser Phe Lys Arg Tyr Gly Cys Val
 225 230 235 240
 Phe Gln Gly Thr Asn Gln Gln Ile Lys Ala His Glu Ala Ser Ser Ala
 245 250 255
 Val Gln His Val Asn Leu Leu Lys Glu Trp Ser Asn Ser Leu Glu Lys
 260 265 270
 Lys Val Ser Leu Leu Gln Asn Glu Ser Val Glu Lys Asn Lys Ser Ile
 275 280 285
 Gln Ser Leu His Asn Gln Ile Cys Ser Phe Glu Ile Glu Ile Glu Arg
 290 295 300
 Gln Lys Glu Met Leu Arg Asn Asn Glu Ser Lys Ile Leu His Leu Gln
 305 310 315 320
 Arg Val Ile Asp Ser Gln Ala Glu Lys Leu Lys Glu Leu Asp Lys Glu
 325 330 335
 Ile Arg Pro Phe Arg Gln Asn Trp Glu Ala Asp Ser Met Lys Ser
 340 345 350
 Ser Val Glu Ser Leu Gln Asn Arg Val Thr Glu Leu Glu Ser Val Asp
 355 360 365
 Lys Ser Ala Gly Gln Val Ala Arg Asn Thr Gly Leu Leu Glu Ser Gln

370 375 380
 Leu Ser Arg His Asp Gln Met Leu Ser Val His Asp Ile Arg Leu Ala 400
 385 390 395
 Asp Met Asp Leu Arg Phe Gln Val Leu Glu Thr Ala Ser Tyr Asn Gly 415
 405 410 415
 Val Leu Ile Trp Lys Ile Arg Asp Tyr Lys Arg Arg Lys Gln Glu Ala 430
 420 425 430
 Val Met Gly Lys Thr Leu Ser Leu Tyr Ser Gln Pro Phe Tyr Thr Gly 445
 435 440 445
 Tyr Phe Gly Tyr Lys Met Cys Ala Arg Val Tyr Leu Asn Gly Asp Gly 460
 450 455 460
 Met Gly Lys Gly Thr His Leu Ser Leu Phe Val Ile Met Arg Gly 480
 465 470 475
 Glu Tyr Asp Ala Leu Leu Pro Trp Pro Phe Lys Gln Lys Val Thr Leu 495
 485 490 495
 Met Leu Met Asp Gln Gly Ser Arg Arg His Leu Gly Asp Ala Phe 510
 500 505 510
 Lys Pro Asp Pro Asn Ser Ser Ser Phe Lys Lys Pro Thr Gly Glu Met 525
 515 520 525
 Asn Ile Ala Ser Gly Cys Pro Val Phe Val Ala Gln Thr Val Leu Glu 540
 530 535 540
 Asn Gly Thr Tyr Ile Lys Asp Asp Thr Ile Phe Ile Lys Val Ile Val 550
 545 550 555
 Asp Thr Ser Asp Leu Pro Asp Pro 565
 560 565 570
 <210> 132
 <211> 197
 <212> PRT
 <213> Homo sapiens
 <400> 132
 Met Pro Ala Pro Ser Met Asp Cys Asp Val Ser Thr Leu Val Ala Cys 15
 1 5 10
 Val Val Asp Val Glu Val Phe Thr Asn Gln Glu Val Lys Glu Lys Phe 30
 20 25 30
 Glu Gly Leu Phe Arg Thr Tyr Asp Asp Cys Val Thr Phe Gln Leu Phe 45
 35 40 45
 Lys Ser Phe Arg Arg Val Arg Ile Asn Phe Ser Asn Pro Lys Ser Ala 60
 50 55 60
 Ala Arg Ala Arg Ile Glu Leu His Glu Thr Gln Phe Arg Gly Lys Lys 80
 65 70 75
 Leu Lys Leu Tyr Phe Ala Gln Val Gln Thr Pro Glu Thr Asp Gly Asp 95
 85 90 95

Lys Leu His Leu Ala Pro Pro Gln Pro Ala Lys Gln Phe Leu Ile Ser 110
 100 105 110
 Pro Pro Ser Ser Pro Pro Val Gly Trp Gln Pro Ile Asn Asp Ala Thr 125
 115 120 125
 Pro Val Leu Asn Tyr Asp Leu Leu Tyr Ala Val Ala Lys Leu Gly Pro 140
 130 135 140
 Gly Glu Lys Tyr Glu Leu His Ala Gly Thr Glu Ser Thr Pro Ser Val 160
 145 150 155
 Val Val His Val Cys Asp Ser Asp Ile Glu Glu Glu Asp Pro Lys 175
 165 170 175
 Thr Ser Pro Lys Pro Lys Ile Ile Gln Thr Arg Arg Pro Gly Leu Pro 190
 180 185 190
 Pro Ser Val Ser Asn 195
 190 195 200
 <210> 133
 <211> 241
 <212> PRT
 <213> Homo sapiens
 <400> 133
 Met Leu Arg Asp Thr Met Lys Ser Trp Asn Asp Ser Gln Ser Asp Leu 15
 1 5 10 15
 Cys Ser Thr Asp Gln Glu Glu Glu Glu Met Ile Phe Gly Glu Asn 30
 20 25 30
 Glu Asp Asp Leu Asp Glu Met Met Asp Leu Ser Asp Leu Pro Thr Ser 45
 35 40 45
 Leu Phe Ala Cys Ser Val His Glu Ala Val Phe Glu Ala Arg Glu Gln 60
 50 55 60
 Lys Glu Arg Phe Glu Ala Leu Phe Thr Ile Tyr Asp Asp Gln Val Thr 80
 65 70 75
 Phe Gln Leu Phe Lys Ser Phe Arg Arg Val Arg Ile Asn Phe Ser Lys 95
 85 90 95
 Pro Glu Ala Ala Arg Ala Arg Ile Glu Leu His Glu Thr Asp Phe 110
 100 105 110
 Asn Gly Gln Lys Leu Lys Leu Tyr Phe Ala Gln Val Gln Met Ser Gly 125
 115 120 125
 Glu Val Arg Asp Lys Ser Tyr Leu Leu Pro Gln Pro Val Lys Gln 140
 130 135 140
 Phe Leu Ile Ser Pro Ala Ser Pro Pro Val Gly Trp Lys Gln Ser 160
 145 150 155
 Glu Asp Ala Met Pro Val Ile Asn Tyr Asp Leu Leu Cys Ala Val Ser 175
 165 170 175
 Lys Leu Gly Pro Gly Glu Lys Tyr Glu Leu His Ala Gly Thr Glu Ser 190
 180 185 190

Thr Pro Ser Val Val His Val Cys Glu Ser Glu Thr Glu Glu
195 200 205
Glu Glu Thr Lys Asn Pro Lys Gln Lys Ile Ala Gln Thr Arg Arg Pro
210 215 220
Asp Pro Pro Thr Ala Ala Leu Asn Glu Pro Gln Thr Phe Asp Cys Ala
225 230 235 240
Leu
<210> 134
<211> 153
<212> PRT
<213> Homo sapiens
<400> 134
Met Ala Val Glu Ser Arg Val Thr Gln Glu Glu Ile Lys Lys Glu Pro
1 5 10 15
Glu Lys Pro Ile Asp Arg Glu Lys Thr Cys Pro Leu Leu Arg Val
20 25 30
Phe Thr Thr Asn Asn Gly Arg His His Arg Met Asp Glu Phe Ser Arg
35 40 45
Gly Asn Val Pro Ser Ser Glu Leu Gln Ile Tyr Thr Trp Met Asp Ala
50 55 60
Thr Leu Lys Glu Leu Thr Ser Leu Val Lys Glu Val Tyr Pro Glu Ala
65 70 75 80
Arg Lys Lys Gly Thr His Phe Asn Phe Ala Ile Val Phe Thr Asp Val
85 90 95
Lys Arg Pro Gly Tyr Arg Val Lys Glu Ile Gly Ser Thr Met Ser Gly
100 105 110
Arg Lys Gly Thr Asp Asp Ser Met Thr Leu Gln Ser Gln Lys Phe Gln
115 120 125
Ile Gly Asp Tyr Leu Asp Ile Ala Ile Thr Pro Pro Asn Arg Ala Pro
130 135 140
Pro Pro Ser Gly Arg Met Arg Pro Tyr
145 150
<210> 135
<211> 692
<212> PRT
<213> Homo sapiens
<400> 135
Met Ser Gln Gln Asp Ala Val Ala Leu Ser Glu Arg Leu Leu Val
1 5 10 15
Ala Ala Tyr Lys Gly Gln Thr Glu Asn Val Val Gln Leu Ile Asn Lys
20 25 30
Gly Ala Arg Val Ala Val Thr Lys His Gly Arg Thr Pro Leu His Leu

271

35 40 45
Ala Ala Asn Lys Gly His Leu Pro Val Val Gln Ile Leu Leu Lys Ala
50 55 60
Gly Cys Asp Leu Asp Val Gln Asp Asp Gly Asp Gln Thr Ala Leu His
65 70 75 80
Arg Ala Thr Val Val Gly Asn Thr Glu Ile Ile Ala Ala Leu Ile His
85 90 95
Glu Gly Cys Ala Leu Asp Arg Gln Asp Lys Asp Gly Asn Thr Ala Leu
100 105 110
His Glu Ala Ser Trp His Gly Phe Ser Gln Ser Ala Lys Leu Val
115 120 125
Lys Ala Gly Ala Asn Val Leu Ala Lys Asn Lys Ala Gly Asn Thr Ala
130 135 140
Leu His Leu Ala Cys Gln Asn Ser His Ser Gln Ser Thr Arg Val Leu
145 150 155 160
Leu Leu Ala Gly Ser Arg Ala Asp Leu Lys Asn Asn Ala Gly Asp Thr
165 170 175
Cys Leu His Val Ala Ala Arg Tyr Asn His Leu Ser Ile Ile Arg Leu
180 185 190
Leu Leu Thr Ala Phe Cys Ser Val His Glu Lys Asn Gln Ala Gly Asp
195 200 205
Thr Ala Leu His Val Ala Ala Leu Asn His Lys Lys Val Ala Lys
210 215 220
Ile Leu Leu Glu Ala Gly Ala Asp Thr Thr Ile Val Asn Asn Ala Gly
225 230 235 240
Gln Thr Pro Leu Glu Thr Ala Arg Tyr His Asn Asn Pro Glu Val Ala
245 250 255
Leu Leu Leu Thr Lys Ala Pro Gln Gly Ser Val Ser Ala Gly Asp Thr
260 265 270
Pro Ser Ser Glu Gln Ala Val Ala Arg Lys Glu Glu Ala Arg Glu Glu
275 280 285
Phe Leu Ser Ala Ser Pro Glu Pro Arg Ala Lys Asp Asp Arg Arg
290 295 300
Lys Ser Arg Pro Lys Val Ser Ala Phe Ser Asp Pro Thr Pro Pro Ala
305 310 315 320
Asp Gln Gln Pro Gly His Gln Lys Asn Leu His Ala His Asn His Pro
325 330 335
Lys Lys Arg Asn Arg His Arg Cys Ser Ser Pro Pro Pro His Glu
340 345 350
Phe Arg Ala Tyr Gln Leu Tyr Thr Leu Tyr Arg Gly Lys Asp Gly Lys
355 360 365

272

Val Met Gln Ala Pro Ile Asn Gly Cys Arg Cys Glu Pro Leu Ile Asn 370 380
 Lys Leu Glu Asn Gln Leu Glu Ala Thr Val Glu Glu Ile Lys Ala Glu 385 390 395 400
 Leu Gly Ser Val Gln Asp Lys Met Asn Thr Lys Leu Gly Gln Met Glu 405 410 415
 Asn Lys Thr Gln His Gln Met Arg Val Leu Asp Lys Leu Met Val Glu 420 425 430
 Arg Leu Ser Ala Glu Arg Thr Glu Cys Leu Asn Arg Leu Gln Gln His 435 440 445 450
 Ser Asp Thr Glu Lys His Glu Gly Glu Lys Arg Gln Ile Ser Leu Val 450 455 460
 Asp Glu Leu Lys Thr Trp Cys Met Leu Lys Ile Gln Asn Leu Glu Gln 465 470 475 480
 Lys Leu Ser Gly Asp Ser Arg Ala Cys Arg Ala Lys Ser Thr Pro Ser 485 490 495
 Thr Cys Glu Ser Ser Thr Gly Val Asp Gln Leu Val Thr Ala Gly 500 505 510
 Pro Ala Ala Ser Asp Ser Ser Pro Val Val Arg Pro Lys Glu 515 520 525
 Lys Ala Leu Asn Ser Thr Ala Thr Gln Arg Leu Gln Gln Glu Leu Ser 530 535 540
 Ser Ser Asp Cys Thr Gly Ser Arg Leu Arg Asn Val Lys Val Gln Thr 545 550 555 560
 Ala Leu Leu Pro Met Asn Glu Ala Ala Arg Ser Asp Gln Gln Ala Gly 565 570 575
 Pro Cys Val Asn Arg Gly Thr Gln Thr Lys Lys Ser Gly Lys Ser Gly 580 585 590
 Pro Thr Arg His Arg Ala Gln Gln Pro Ala Ala Ser Ser Thr Cys Gly 595 600 605
 Gln Pro Pro Ala Thr Gly Ser Glu Gln Thr Gly Pro His Ile Arg 610 615 620
 Asp Thr Ser Gln Ala Leu Glu Leu Thr Gln Tyr Phe Phe Glu Ala Val 625 630 635 640
 Ser Thr Gln Met Glu Lys Trp Tyr Glu Arg Lys Ile Glu Glu Ala Arg 645 650 655
 Ser Gln Ala Asn Gln Lys Ala Gln Gln Asp Lys Ala Thr Leu Lys Glu 660 665 670
 His Ile Lys Ser Leu Glu Glu Leu Ala Lys Leu Arg Thr Arg Val 675 680 685
 Gln Lys Glu Asn 690

273

<210> 136
 <211> 556
 <212> PRT
 <213> Homo sapiens
 <400> 136
 Met Ala Arg Thr Thr Ser Gln Leu Tyr Asp Ala Val Pro Ile Gln Ser 1 5 10 15
 Ser Val Val Leu Cys Ser Cys Pro Ser Pro Ser Met Val Arg Thr Gln 20 25 30
 Thr Glu Ser Ser Thr Pro Pro Gly Ile Pro Gly Gly Ser Arg Gln Gly 35 40 45
 Pro Ala Met Asp Gly Thr Ala Ala Glu Pro Arg Pro Gly Ala Gly Ser 50 55 60
 Leu Gln His Ala Gln Pro Pro Gln Pro Arg Lys Lys Arg Pro Glu 65 70 75 80
 Asp Phe Lys Phe Gly Lys Ile Leu Gly Glu Gly Ser Phe Ser Thr Val 85 90 95
 Val Leu Ala Arg Glu Leu Ala Thr Ser Arg Glu Tyr Ala Ile Lys Ile 100 105 110
 Leu Glu Lys Arg His Ile Ile Lys Glu Asn Lys Val Pro Tyr Val Thr 115 120 125
 Arg Glu Arg Asp Val Met Ser Arg Leu Asp His Pro Phe Val Lys 130 135 140
 Leu Tyr Phe Thr Phe Gln Asp Asp Glu Lys Leu Tyr Phe Gly Leu Ser 145 150 155 160
 Tyr Ala Lys Asn Gly Glu Leu Lys Tyr Ile Arg Lys Ile Gly Ser 165 170 175
 Phe Asp Glu Thr Cys Thr Arg Phe Tyr Thr Ala Glu Ile Val Ser Ala 180 185 190
 Leu Glu Tyr Leu His Gly Lys Gly Ile Ile His Arg Asp Leu Lys Pro 195 200 205
 Glu Asn Ile Leu Leu Asn Glu Asp Met His Ile Gln Ile Thr Asp Phe 210 215 220
 Gly Thr Ala Lys Val Leu Ser Pro Glu Ser Lys Gln Ala Arg Ala Asn 225 230 235 240
 Ser Phe Val Gly Thr Ala Gln Tyr Val Ser Pro Glu Leu Thr Glu 245 250 255
 Lys Ser Ala Cys Lys Ser Ser Asp Leu Trp Ala Leu Gly Cys Ile Ile 260 265 270
 Tyr Gln Leu Val Ala Gly Leu Pro Pro Phe Arg Ala Gly Asn Glu Tyr 275 280 285
 Leu Ile Phe Gln Lys Ile Ile Lys Leu Glu Tyr Asp Phe Pro Glu Lys

274

290 295 300
 Phe Phe Pro Lys Ala Arg Asp Leu Val Glu Lys Leu Leu Val Leu Asp 320
 305 310 315
 Ala Thr Lys Arg Leu Gly Cys Glu Met Glu Gly Tyr Gly Pro Leu 335
 325 330
 Lys Ala His Pro Phe Phe Glu Ser Val Thr Trp Glu Asn Leu His Gln 350
 340 345
 Gln Thr Pro Pro Lys Leu Thr Ala Tyr Leu Pro Ala Met Ser Glu Asp 365
 355 360
 Asp Glu Asp Cys Tyr Gly Asn Tyr Asp Asn Leu Leu Ser Gln Phe Gly 380
 370 375
 Cys Met Gln Val Ser Ser Ser Ser Ser His Ser Leu Ser Ala Ser 400
 385 390 395
 Asp Thr Gly Leu Pro Gln Arg Ser Gly Ser Asn Ile Glu Gln Tyr Ile 415
 405 410
 His Asp Leu Asp Ser Asn Ser Phe Glu Leu Asp Leu Gln Phe Ser Glu 430
 420 425
 Asp Glu Lys Arg Leu Leu Glu Lys Gln Ala Gly Gly Asn Pro Trp 445
 435 440
 His Gln Phe Val Glu Asn Asn Leu Ile Leu Lys Met Gly Pro Val Asp 460
 450 455
 Lys Arg Lys Gly Leu Phe Ala Arg Arg Gln Gln Leu Leu Thr Glu 480
 465 470 475
 Gly Pro His Leu Tyr Tyr Val Asp Pro Val Asn Lys Val Leu Lys Gly 495
 485 490
 Glu Ile Pro Trp Ser Gln Glu Leu Arg Pro Glu Ala Lys Asn Phe Lys 510
 500 505
 Thr Phe Phe Val His Thr Pro Asn Arg Thr Tyr Tyr Leu Met Asp Pro 525
 515 520
 Ser Gly Asn Ala His Lys Trp Cys Arg Lys Ile Gln Glu Val Trp Arg 540
 530 535
 Gln Arg Tyr Gln Ser His Pro Asp Ala Ala Val Gln 555
 545 550
 <210> 137
 <211> 279
 <212> PRT
 <213> Homo sapiens
 <400> 137
 Met Glu Ala Val Val Asn Leu Tyr Gln Glu Val Met Lys His Ala Asp 15
 1 5 10
 Pro Arg Ile Gln Gly Tyr Pro Leu Met Gly Ser Pro Leu Leu Met Thr 30
 20 25

275

Ser Ile Leu Leu Thr Tyr Val Tyr Phe Val Leu Ser Leu Gly Pro Arg 45
 35 40
 Ile Met Ala Asn Arg Lys Pro Phe Gln Leu Arg Gly Phe Met Ile Val 60
 50 55
 Tyr Asn Phe Ser Leu Val Ala Leu Ser Leu Tyr Ile Val Tyr Glu Phe 80
 65 70 75
 Leu Met Ser Gly Trp Leu Ser Thr Tyr Trp Arg Cys Asp Pro Val 95
 85 90
 Asp Tyr Ser Asn Ser Pro Glu Ala Leu Arg Met Val Arg Val Ala Trp 110
 100 105
 Leu Phe Leu Phe Ser Lys Phe Ile Glu Leu Met Asp Thr Val Ile Phe 125
 115 120
 Ile Leu Arg Lys Lys Asp Gly Gln Val Thr Phe Leu His Val Phe His 140
 130 135
 His Ser Val Leu Pro Trp Ser Trp Trp Gly Val Lys Ile Ala Pro 160
 145 150 155
 Gly Gly Met Gly Ser Phe His Ala Met Ile Asn Ser Ser Val His Val 175
 165 170
 Ile Met Tyr Leu Tyr Tyr Gly Leu Ser Ala Phe Gly Pro Val Ala Gln 190
 180 185
 Pro Tyr Leu Trp Trp Lys Lys His Met Thr Ala Ile Gln Leu Ile Gln 205
 195 200
 Phe Val Leu Val Ser Leu His Ile Ser Gln Tyr Tyr Phe Met Ser Ser 220
 210 215
 Cys Asn Tyr Gln Tyr Pro Val Ile Ile His Leu Ile Trp Met Tyr Gly 240
 225 230 235
 Thr Ile Phe Phe Met Leu Phe Ser Asn Phe Trp Tyr His Ser Tyr Thr 255
 245 250
 Lys Gly Lys Arg Leu Pro Arg Ala Leu Gln Asn Gly Ala Pro Gly 270
 260 265
 Ile Ala Lys Val Lys Ala Asn 275
 270
 <210> 138
 <211> 324
 <212> PRT
 <213> Homo sapiens
 <400> 138
 Asp Ser Ala Gly Gln Arg Asp Pro Ala Thr Leu Asp Ser Ala Ser Pro 15
 1 5 10
 Pro Ala Arg Val Ala Ala Pro Gln Pro Leu Arg Ile Met Glu His Leu 30
 20 25
 Lys Ala Phe Asp Asp Glu Ile Asn Ala Phe Leu Asp Asn Met Phe Gly 45
 35 40

276

Pro Arg Asp Ser Arg Val Arg Gly Trp Phe Met Leu Asp Ser Tyr Leu
50 55 60

Pro Thr Phe Phe Leu Thr Val Met Tyr Leu Leu Ser Ile Trp Leu Gly
65 70 75 80

Asn Lys Tyr Met Lys Asn Arg Pro Ala Leu Ser Leu Arg Gly Ile Leu
85 90 95

Thr Leu Tyr Asn Leu Gly Ile Thr Leu Leu Ser Ala Tyr Met Leu Ala
100 105 110

Glu Leu Ile Leu Ser Thr Trp Gly Gly Tyr Asn Leu Gln Cys Gln
115 120 125

Asp Leu Thr Ser Ala Gly Glu Ala Asp Ile Arg Val Ala Lys Val Leu
130 135 140

Trp Trp Tyr Tyr Phe Ser Lys Ser Val Glu Phe Leu Asp Thr Ile Phe
145 150 155 160

Phe Val Leu Arg Lys Lys Thr Ser Gln Ile Thr Phe Leu His Val Tyr
165 170 175

His His Ala Ser Met Phe Asn Ile Trp Trp Cys Val Leu Asn Trp Ile
180 185 190

Pro Cys Gly Gln Ser Phe Phe Gly Pro Thr Leu Asn Ser Phe Ile His
195 200 205

Ile Leu Met Tyr Ser Tyr Tyr Gly Leu Ser Val Phe Pro Ser Met His
210 215 220

Lys Tyr Leu Trp Trp Lys Lys Tyr Leu Thr Gln Ala Gln Leu Val Gln
225 230 235 240

Phe Val Leu Thr Ile Thr His Thr Met Ser Ala Val Val Lys Pro Cys
245 250 255

Gly Phe Pro Phe Gly Cys Leu Ile Phe Gln Ser Ser Tyr Met Leu Thr
260 265 270

Leu Val Ile Leu Phe Leu Asn Phe Tyr Gln Gln Thr Tyr Arg Lys Lys
275 280 285

Pro Met Lys Lys Asp Met Gln Glu Pro Pro Ala Gly Lys Glu Val Lys
290 295 300

Asn Gly Phe Ser Lys Ala Tyr Phe Thr Ala Ala Asn Gly Val Met Asn
305 310 315 320

Lys Lys Ala Gln

<210> 139
<211> 744
<212> PRT
<213> Homo sapiens
<400> 139
Met Ala Ser Glu Gly Thr Asn Ile Pro Ser Pro Val Val Arg Gln Ile

277

1 5 10 15

Asp Lys Gln Phe Leu Ile Cys Ser Ile Cys Leu Glu Arg Tyr Tyr Asn
20 25 30

Pro Lys Val Leu Pro Cys Leu His Thr Phe Cys Glu Arg Cys Leu Gln
35 40 45

Asn Tyr Ile Pro Ala His Ser Leu Thr Leu Ser Cys Pro Val Cys Arg
50 55 60

Gln Thr Ser Ile Leu Pro Glu Lys Gly Val Ala Ala Leu Gln Asn Asn
65 70 75 80

Phe Phe Ile Thr Asn Leu Met Asp Val Leu Gln Arg Thr Pro Gly Ser
85 90 95

Asn Ala Glu Glu Ser Ser Ile Leu Glu Thr Val Thr Ala Val Ala Ala
100 105 110

Gly Lys Pro Leu Ser Cys Pro Asn His Asp Gly Asn Val Met Glu Phe
115 120 125

Tyr Cys Gln Ser Cys Glu Thr Ala Met Cys Arg Glu Cys Thr Glu Gly
130 135 140

Glu His Ala Glu His Pro Thr Val Pro Leu Lys Asp Val Val Glu Gln
145 150 155 160

His Lys Ala Ser Leu Gln Val Gln Leu Asp Ala Val Asn Lys Arg Leu
165 170 175

Pro Glu Ile Asp Ser Ala Leu Gln Phe Ile Ser Glu Ile Ile His Gln
180 185 190

Leu Thr Asn Gln Lys Ala Ser Ile Val Asp Asp Ile His Ser Thr Phe
195 200 205

Asp Glu Leu Gln Lys Thr Leu Asn Val Arg Lys Ser Val Leu Leu Met
210 215 220

Glu Leu Glu Val Asn Tyr Gly Leu Lys His Lys Val Leu Gln Ser Gln
225 230 235 240

Leu Asp Thr Leu Leu Gln Gly Gln Glu Ser Ile Lys Ser Cys Ser Asn
245 250 255

Phe Thr Ala Gln Ala Leu Asn His Gly Thr Glu Thr Glu Val Leu Leu
260 265 270

Val Lys Lys Gln Met Ser Glu Lys Leu Asn Glu Leu Ala Asp Gln Asp
275 280 285

Phe Pro Leu His Pro Arg Glu Asn Asp Gln Leu Asp Phe Ile Val Glu
290 295 300

Thr Glu Gly Leu Lys Ser Ile His Asn Leu Gly Thr Ile Leu Thr
305 310 315 320

Thr Asn Ala Val Ala Ser Glu Thr Val Ala Thr Gly Glu Gly Leu Arg
325 330 335

278

Gln Thr Ile Ile Gly Gln Pro Met Ser Val Thr Thr Thr Thr Lys Asp
340 345 350
Lys Asp Gly Gln Leu Cys Lys Thr Gly Asn Ala Tyr Leu Thr Ala Glu
355 360 365
Leu Ser Thr Pro Asp Gly Ser Val Ala Asp Gly Glu Ile Leu Asp Asn
370 375 380
Lys Asn Gly Thr Tyr Glu Phe Leu Tyr Thr Val Gln Lys Glu Gly Asp
385 390 395 400
Phe Thr Leu Ser Leu Arg Leu Tyr Asp Gln His Ile Arg Gly Ser Pro
405 410 415
Phe Lys Leu Lys Val Ile Arg Ser Ala Asp Val Ser Pro Thr Thr Glu
420 425 430
Gly Val Lys Arg Arg Val Lys Ser Pro Gly Ser Gly His Val Lys Gln
435 440 445
Lys Ala Val Lys Arg Pro Ala Ser Met Tyr Ser Thr Gly Lys Arg Lys
450 455 460
Glu Asn Pro Ile Glu Asp Asp Leu Ile Phe Arg Val Gly Thr Lys Gly
465 470 475 480
Arg Asn Lys Gly Glu Phe Thr Asn Leu Gln Gly Val Ala Ala Ser Thr
485 490 495
Asn Gly Lys Ile Leu Ile Ala Asp Ser Asn Asn Gln Cys Val Gln Ile
500 505 510
Phe Ser Asn Asp Gly Gln Phe Lys Ser Arg Phe Gly Ile Arg Gly Arg
515 520 525
Ser Pro Gly Gln Leu Gln Arg Pro Thr Gly Val Ala Val His Pro Ser
530 535 540
Gly Asp Ile Ile Ile Ala Asp Tyr Asp Asn Lys Trp Val Ser Ile Phe
545 550 555 560
Ser Ser Asp Gly Lys Phe Lys Thr Lys Ile Gly Ser Gly Lys Leu Met
565 570 575
Gly Pro Lys Gly Val Ser Val Asp Arg Asn Gly His Ile Ile Val Val
580 585 590
Asp Asn Lys Ala Cys Cys Val Phe Ile Phe Gln Pro Asn Gly Lys Ile
595 600 605
Val Thr Arg Phe Gly Ser Arg Gly Asn Gly Asp Arg Gln Phe Ala Gly
610 615 620
Pro His Phe Ala Ala Val Asn Ser Asn Asn Glu Ile Ile Ile Thr Asp
625 630 635 640
Phe His Asn His Ser Val Lys Val Phe Asn Gln Glu Gly Glu Phe Met
645 650 655
Leu Lys Phe Gly Ser Asn Gly Glu Gly Asn Gly Gln Phe Asn Ala Pro
660 665 670

279

Thr Gly Val Ala Val Asp Ser Asn Gly Asn Ile Ile Val Ala Asp Trp
675 680 685
Gly Asn Ser Arg Ile Gln Val Phe Asp Gly Ser Gly Ser Phe Leu Ser
690 695 700
Tyr Ile Asn Thr Ser Ala Asp Pro Leu Tyr Gly Pro Gln Gly Leu Ala
705 710 715 720
Leu Thr Ser Asp Gly His Val Val Ala Asp Ser Gly Asn His Cys
725 730 735
Phe Lys Val Tyr Arg Tyr Leu Gln
740
<210> 140
<211> 744
<212> PRT
<213> Homo sapiens
<400> 140
Met Ala Ser Glu Gly Thr Asn Ile Pro Ser Pro Val Val Arg Gln Ile
1 5 10 15
Asp Lys Gln Phe Leu Ile Cys Ser Ile Cys Ser Leu Glu Arg Tyr Lys Asn
20 25 30
Pro Lys Val Leu Pro Cys Leu His Thr Phe Cys Glu Arg Cys Leu Gln
35 40 45
Asn Tyr Ile Pro Ala His Ser Leu Thr Leu Ser Cys Pro Val Cys Arg
50 55 60
Gln Thr Ser Ile Leu Pro Glu Lys Gly Val Ala Ala Leu Gln Asn Asn
65 70 75 80
Phe Phe Ile Thr Asn Leu Met Asp Val Leu Gln Arg Thr Pro Gly Ser
85 90 95
Asn Ala Glu Glu Ser Ser Ile Leu Glu Thr Val Thr Ala Val Ala Ala
100 105 110
Gly Lys Pro Leu Ser Cys Pro Asn His Asp Gly Asn Val Met Glu Phe
115 120 125
Tyr Cys Gln Ser Cys Glu Thr Ala Met Cys Arg Glu Cys Thr Glu Gly
130 135 140
Glu His Ala Glu His Pro Thr Val Pro Leu Lys Asp Val Val Glu Gln
145 150 155 160
His Lys Ala Ser Leu Gln Val Gln Leu Asp Ala Val Asn Lys Arg Leu
165 170 175
Pro Glu Ile Asp Ser Ala Leu Gln Phe Ile Ser Glu Ile Ile His Gln
180 185 190
Leu Thr Asn Gln Lys Ala Ser Ile Val Asp Asp Ile His Ser Thr Phe
195 200 205
Asp Glu Leu Gln Lys Thr Leu Asn Val Arg Lys Ser Val Leu Leu Met
280

210 220
 Glu Leu Glu Val Asn Tyr Gly Leu Lys His Lys Val Leu Gln Ser Gln 240
 225 230 235
 Leu Asp Thr Leu Leu Gln Gly Gln Glu Ser Ile Lys Ser Cys Ser Asn 255
 245 250
 Phe Thr Ala Gln Ala Leu Asn His Gly Thr Glu Thr Glu Val Leu Leu 270
 260 265
 Val Lys Lys Gln Met Ser Glu Lys Leu Asn Glu Leu Ala Asp Gln Asp 285
 275 280
 Phe Pro Leu His Pro Arg Glu Asn Asp Gln Leu Asp Phe Ile Val Glu 300
 290 295
 Thr Glu Gly Leu Lys Lys Ser Ile His Asn Leu Gly Thr Ile Leu Thr 320
 305 310 315
 Thr Asn Ala Val Ala Ser Glu Thr Val Ala Thr Gly Glu Gly Leu Arg 335
 325 330
 Gln Thr Ile Ile Gly Gln Pro Met Ser Val Thr Ile Thr Thr Lys Asp 350
 340 345
 Lys Asp Gly Glu Leu Cys Lys Thr Gly Asn Ala Tyr Leu Thr Ala Glu 365
 355 360
 Leu Ser Thr Pro Asp Gly Ser Val Ala Asp Gly Glu Ile Leu Asp Asn 380
 370 375
 Lys Asn Gly Thr Tyr Glu Phe Leu Tyr Thr Val Gln Lys Glu Gly Asp 400
 385 390 395
 Phe Thr Leu Ser Leu Arg Leu Tyr Asp Gln His Ile Arg Gly Ser Pro 415
 405 410
 Phe Lys Leu Lys Val Ile Arg Ser Ala Asp Val Ser Pro Thr Thr Glu 430
 420 425
 Gly Val Lys Arg Arg Val Lys Ser Pro Gly Ser Gly His Val Lys Gln 445
 435 440
 Lys Ala Val Lys Arg Pro Ala Ser Met Tyr Ser Thr Gly Lys Arg Lys 460
 450 455
 Glu Asn Pro Ile Glu Asp Asp Leu Ile Phe Arg Val Gly Thr Lys Gly 480
 465 470 475
 Arg Asn Lys Gly Glu Phe Thr Asn Leu Gln Gly Val Ala Ala Ser Thr 495
 485 490
 Asn Gly Lys Ile Leu Ile Ala Asp Ser Asn Asn Gln Cys Val Gln Ile 510
 500 505
 Phe Ser Asn Asp Gly Gln Phe Lys Ser Arg Phe Gly Ile Arg Gly Arg 525
 515 520
 Ser Pro Gly Gln Leu Cln Arg Pro Thr Gly Val Ala Val His Pro Ser 540
 530 535

Gly Asp Ile Ile Ile Ala Asp Tyr Asp Asn Lys Trp Val Ser Ile Phe 550
 545 555
 Ser Ser Asp Gly Lys Phe Lys Thr Lys Ile Gly Ser Gly Lys Leu Met 575
 565 570
 Gly Pro Lys Gly Val Ser Val Asp Arg Asn Gly His Ile Ile Val Val 590
 580 585
 Asp Asn Lys Ala Cys Cys Val Phe Ile Phe Gln Pro Asn Gly Lys Ile 605
 595 600
 Val Thr Arg Phe Gly Ser Arg Gly Asn Gly Asp Arg Gln Phe Ala Gly 620
 610 615
 Pro His Phe Ala Ala Val Asn Ser Asn Asn Glu Ile Ile Ile Thr Asp 640
 625 630 635
 Phe His Asn His Ser Val Lys Val Phe Asn Gln Glu Gly Glu Phe Met 655
 645 650
 Leu Lys Phe Gly Ser Asn Gly Glu Gly Asn Gly Gln Phe Asn Ala Pro 670
 660 665
 Thr Gly Val Ala Val Asp Ser Asn Gly Asn Ile Ile Val Ala Asp Trp 685
 675 680
 Gly Asn Ser Arg Ile Gln Val Phe Asp Gly Ser Gly Ser Phe Leu Ser 700
 690 695
 Tyr Ile Asn Thr Ser Ala Asp Pro Leu Tyr Gly Pro Gln Gly Leu Ala 720
 705 710 715
 Leu Thr Ser Asp Gly His Val Val Ala Asp Ser Gly Asn His Cys 735
 725 730
 Phe Lys Val Tyr Arg Tyr Leu Gln 740
 745
 <210> 141
 <211> 423
 <212> PRT
 <213> Homo sapiens
 <400> 141
 Met Val Phe Ser Asn Asn Asp Glu Gly Leu Ile Asn Lys Lys Leu Pro 15
 1 5 10
 Lys Glu Leu Leu Arg Ile Phe Ser Phe Leu Asp Ile Val Thr Leu 30
 20 25
 Cys Arg Cys Ala Gln Ile Ser Lys Ala Trp Asn Ile Leu Ala Leu Asp 45
 35 40
 Gly Ser Asn Trp Gln Arg Ile Asp Leu Phe Asn Phe Gln Thr Asp Val 60
 50 55
 Glu Gly Arg Val Val Glu Asn Ile Ser Lys Arg Cys Gly Gly Phe Leu 80
 65 70 75
 Arg Lys Leu Ser Leu Arg Gly Cys Ile Gly Val Gly Asp Ser Ser Leu 95
 85 90

Lys Thr Phe Ala Gln Asn Cys Arg Asn Ile Glu His Leu Asn Leu Asn
 100 105 110
 Gly Cys Thr Lys Ile Thr Asp Ser Thr Cys Tyr Ser Leu Ser Arg Phe
 115 120 125
 Cys Ser Lys Leu Lys His Leu Asp Leu Thr Ser Cys Val Ser Ile Thr
 130 135 140
 Asn Ser Ser Leu Lys Gly Ile Ser Glu Gly Cys Arg Asn Leu Glu Tyr
 145 150 155 160
 Leu Asn Leu Ser Trp Cys Asp Gln Ile Thr Lys Asp Gly Ile Glu Ala
 165 170 175
 Leu Val Arg Gly Cys Arg Gly Leu Lys Ala Leu Leu Arg Gly Cys
 180 185 190
 Thr Gln Leu Glu Asp Glu Ala Leu Lys His Ile Gln Asn Tyr Cys His
 195 200 205
 Glu Leu Val Ser Leu Asn Leu Gln Ser Cys Ser Arg Ile Thr Asp Glu
 210 215 220
 Gly Val Val Gln Ile Cys Arg Gly Cys His Arg Leu Gln Ala Leu Cys
 225 230 235 240
 Leu Ser Gly Cys Ser Asn Leu Thr Asp Ala Ser Leu Thr Ala Leu Gly
 245 250 255
 Leu Asn Cys Pro Arg Leu Gln Ile Leu Glu Ala Ala Arg Cys Ser His
 260 265 270
 Leu Thr Asp Ala Gly Phe Thr Leu Leu Ala Arg Asn Cys His Glu Leu
 275 280 285
 Glu Lys Met Asp Leu Glu Glu Cys Ile Leu Ile Thr Asp Ser Thr Leu
 290 295 300
 Ile Gln Leu Ser Ile His Cys Pro Lys Leu Gln Ala Leu Ser Leu Ser
 305 310 315 320
 His Cys Glu Leu Ile Thr Asp Asp Gly Ile Leu His Leu Ser Asn Ser
 325 330 335
 Thr Cys Gly His Glu Arg Leu Arg Val Leu Glu Leu Asp Asn Cys Leu
 340 345 350
 Leu Ile Thr Asp Val Ala Leu Glu His Leu Glu Asn Cys Arg Gly Leu
 355 360 365
 Glu Arg Leu Glu Leu Tyr Asp Cys Gln Gln Val Thr Arg Ala Gly Ile
 370 375 380
 Lys Arg Met Arg Ala Gln Leu Pro His Val Lys Val His Ala Tyr Phe
 385 390 395 400
 Ala Pro Val Thr Pro Thr Ala Val Ala Gly Ser Gly Gln Arg Leu
 405 410 415
 Cys Arg Cys Cys Val Ile Leu

283

420

<210> 142
 <211> 499
 <212> PRT
 <213> Homo sapiens
 <400> 142
 Pro Gly Lys Glu Asn Ile Asn Asp Glu Pro Val Asp Met Ser Ala Arg
 1 5 10 15
 Arg Ser Glu Pro Glu Arg Gly Arg Leu Thr Pro Ser Pro Asp Ile Ile
 20 25 30
 Val Leu Ser Asp Asn Glu Ala Ser Ser Pro Arg Ser Ser Arg Met
 35 40 45
 Glu Glu Arg Leu Lys Ala Ala Asn Leu Glu Met Phe Lys Gly Lys Gly
 50 55 60
 Ile Glu Glu Arg Gln Gln Leu Ile Lys Gln Leu Arg Asp Glu Leu Arg
 65 70 75 80
 Leu Glu Glu Ala Arg Leu Val Leu Leu Lys Lys Leu Arg Gln Ser Gln
 85 90 95
 Leu Gln Lys Glu Asn Val Val Gln Lys Thr Pro Val Val Gln Asn Ala
 100 105 110
 Ala Ser Ile Val Gln Pro Ser Pro Ala His Val Gly Gln Gln Gly Leu
 115 120 125
 Ser Lys Leu Pro Ser Arg Pro Gly Ala Gln Gly Val Glu Pro Gln Asn
 130 135 140
 Leu Arg Thr Leu Gln Gly His Ser Val Ile Arg Ser Ala Thr Asn Thr
 145 150 155 160
 Thr Leu Pro His Met Leu Met Ser Gln Arg Val Ile Ala Pro Asn Pro
 165 170 175
 Ala Gln Leu Gln Gly Gln Arg Gly Pro Pro Lys Pro Gly Leu Val Arg
 180 185 190
 Thr Thr Thr Pro Asn Met Asn Pro Ala Ile Asn Tyr Gln Pro Gln Ser
 195 200 205
 Ser Ser Ser Val Pro Cys Gln Arg Thr Thr Ser Ser Ala Ile Tyr Met
 210 215 220
 Asn Leu Ala Ser His Ile Gln Pro Gly Thr Val Asn Arg Val Ser Ser
 225 230 235 240
 Pro Leu Pro Ser Pro Ser Ala Met Thr Asp Ala Ala Asn Ser Gln Ala
 245 250 255
 Ala Ala Lys Leu Ala Leu Arg Lys Gln Leu Glu Lys Thr Leu Leu Glu
 260 265 270
 Ile Pro Pro Pro Lys Pro Pro Ala Pro Leu Leu His Phe Leu Pro Ser
 275 280 285

284

Ala Ala Ser Glu Phe Ile Tyr Met Val Gly Leu Glu Val Val
290 300
Gln Ser Val Ile Asp Ser Gln Gly Lys Ser Cys Ala Ser Leu Leu Arg
305 310 315 320
Val Glu Pro Phe Val Cys Ala Gln Cys Arg Thr Asp Phe Thr Pro His
325 330 335
Trp Lys Gln Glu Lys Asn Gly Lys Ile Leu Cys Glu Gln Cys Met Thr
340 345 350
Ser Asn Gln Lys Lys Ala Leu Lys Ala Glu His Thr Asn Arg Leu Lys
355 360 365
Asn Ala Phe Val Lys Ala Leu Gln Gln Glu Ile Glu Gln Arg
370 375 380
Leu Gln Gln Gln Ala Ala Leu Ser Pro Thr Thr Ala Pro Ala Val Ser
385 390 395 400
Ser Val Ser Lys Gln Glu Thr Ile Met Arg His His Thr Leu Arg Gln
405 410 415
Ala Pro Gln Pro Gln Ser Ser Leu Gln Arg Gly Ile Pro Thr Ser Ala
420 425 430
Arg Ser Met Leu Ser Asn Phe Ala Gln Ala Pro Gln Leu Ser Val Pro
435 440 445
Gly Gly Leu Leu Gly Met Pro Gly Val Asn Ile Ala Tyr Leu Asn Thr
450 455 460
Gly Ile Gly Gly His Lys Gly Pro Ser Leu Ala Asp Arg Gln Arg Glu
465 470 475 480
Tyr Leu Leu Asp Met Ile Pro Pro Arg Ser Ile Ser Gln Ser Ile Ser
485 490 495
Gly Gln Lys

<210> 143
<211> 265
<212> PRT
<213> Homo sapiens

<400> 143
Met Asn Met Ser Val Leu Thr Leu Gln Glu Tyr Glu Phe Glu Lys Gln
1 5 10 15
Phe Asn Glu Asn Glu Ala Ile Gln Trp Met Gln Glu Asn Trp Lys Lys
20 25 30
Ser Phe Leu Phe Ser Ala Leu Tyr Ala Ala Phe Ile Phe Gly Gly Arg
35 40 45
His Leu Met Asn Lys Arg Ala Lys Phe Glu Leu Arg Lys Pro Leu Val
50 55 60
Leu Trp Ser Leu Thr Leu Ala Val Phe Ser Ile Phe Gly Ala Leu Arg
65 70 75 80

285

Thr Gly Ala Tyr Met Val Tyr Ile Leu Met Thr Lys Gly Leu Lys Gln
85 90 95
Ser Val Cys Asp Gln Gly Phe Tyr Asn Gly Pro Val Ser Lys Phe Trp
100 105 110
Ala Tyr Ala Phe Val Leu Ser Lys Ala Pro Glu Leu Gly Asp Thr Ile
115 120 125
Phe Ile Ile Leu Arg Lys Gln Lys Leu Ile Phe Leu His Trp Tyr His
130 135 140
His Ile Thr Val Leu Leu Tyr Ser Trp Tyr Lys Asp Met Val
145 150 155 160
Ala Gly Gly Gly Trp Phe Met Thr Met Asn Tyr Gly Val His Ala Val
165 170 175
Met Tyr Ser Tyr Tyr Ala Leu Arg Ala Ala Gly Phe Arg Val Ser Arg
180 185 190
Lys Phe Ala Met Phe Ile Thr Leu Ser Gln Ile Thr Gln Met Leu Met
195 200 205
Gly Cys Val Val Asn Tyr Leu Val Phe Cys Trp Met Gln His Asp Gln
210 215 220
Cys His Ser His Phe Gln Asn Ile Phe Trp Ser Ser Leu Met Tyr Leu
225 230 235 240
Ser Tyr Leu Val Leu Phe Cys His Phe Phe Glu Ala Tyr Ile Gly
245 250 255
Lys Met Arg Lys Thr Thr Lys Ala Glu
260 265

<210> 144
<211> 351
<212> PRT
<213> Homo sapiens

<400> 144
Met Gln Arg Ala Leu Pro Gly Ala Arg Gln His Leu Gly Ala Ile Leu
1 5 10 15
Ala Ser Ala Ser Val Val Val Lys Ala Leu Cys Ala Ala Val Leu Phe
20 25 30
Leu Tyr Leu Leu Ser Phe Ala Val Asp Thr Gly Cys Leu Ala Val Thr
35 40 45
Pro Gly Tyr Leu Phe Pro Asn Phe Trp Ile Trp Thr Leu Ala Thr
50 55 60
His Gly Leu Met Glu Gln His Val Trp Asp Val Ala Ile Ser Leu Thr
65 70 75 80
Thr Val Val Val Ala Gly Arg Leu Leu Glu Pro Leu Trp Gly Ala Leu
85 90 95
Glu Leu Leu Ile Phe Phe Ser Val Val Asn Val Ser Val Gly Leu Leu
286

100 105 110
 Gly Ala Phe Ala Tyr Leu Leu Thr Tyr Met Ala Ser Phe Asn Leu Val
 115 120 125
 Tyr Leu Phe Thr Val Arg Ile His Gly Ala Leu Gly Phe Leu Gly Gly
 130 135 140
 Val Leu Val Ala Leu Lys Gln Thr Met Gly Asp Cys Val Val Leu Arg
 145 150 155 160
 Val Pro Gln Val Arg Val Ser Val Met Pro Met Leu Leu Leu Ala Leu
 165 170 175
 Leu Leu Leu Arg Leu Ala Thr Leu Leu Gln Ser Pro Ala Leu Ala
 180 185 190
 Ser Tyr Gly Phe Gly Leu Leu Ser Ser Trp Val Tyr Leu Arg Phe Tyr
 195 200 205
 Gln Arg His Ser Arg Gly Arg Gly Asp Met Ala Asp His Phe Ala Phe
 210 215 220
 Ala Thr Phe Phe Pro Gln Ile Leu Gln Pro Val Val Gly Leu Leu Ala
 225 230 235 240
 Asn Leu Val His Ser Leu Leu Val Lys Val Lys Ile Cys Gln Lys Thr
 245 250 255
 Val Lys Arg Tyr Asp Val Gly Ala Pro Ser Ser Ile Thr Ile Ser Leu
 260 265 270
 Pro Gly Thr Asp Pro Gln Asp Ala Gln Arg Arg Gln Leu Leu Leu
 275 280 285
 Lys Ala Leu Asn Gln Arg Leu Lys Arg Val Gln Asp Gln Ser Ile Trp
 290 295 300
 Pro Ser Met Asp Asp Asp Gln Gln Ser Gly Ala Lys Val Asp Ser
 305 310 315 320
 Pro Leu Pro Ser Asp Lys Ala Pro Thr Pro Gly Lys Gly Ala Ala
 325 330 335
 Pro Gln Ser Ser Leu Ile Thr Phe Gln Ala Ala Pro Pro Thr Leu
 340 345 350
 <210> 145
 <211> 315
 <212> PRT
 <213> Homo sapiens
 <400> 145
 Met Gln Ala Arg Ala Gln Ser Gly Asn Gly Ser Gln Pro Leu Leu Gln
 1 5 10 15
 Thr Pro Arg Asp Gly Gly Arg Gln Arg Gly Gln Pro Asp Pro Arg Asp
 20 25 30
 Ala Leu Thr Gln Gln Val His Val Leu Ser Leu Asp Gln Ile Arg Ala
 35 40 45

Ile Arg Asn Thr Asn Gln Tyr Thr Gln Gly Pro Thr Val Val Pro Arg
 50 55 60
 Pro Gly Leu Lys Pro Ala Pro Arg Pro Ser Thr Gln His Lys His Gln
 65 70 75 80
 Arg Leu His Gly Leu Pro Gln His Arg Gln Pro Pro Arg Leu Gln His
 85 90 95
 Ser Gln Val His Ser Ser Ala Arg Ala Pro Leu Ser Arg Ser Ile Ser
 100 105 110
 Thr Val Ser Ser Gly Ser Arg Ser Thr Arg Thr Ser Thr Ser Ser
 115 120 125
 Ser Ser Ser Gln Gln Arg Leu Leu Gly Ser Ser Phe Ser Ser Gly Pro
 130 135 140
 Val Ala Asp Gly Ile Ile Arg Val Gln Pro Lys Ser Gln Leu Lys Pro
 145 150 155 160
 Gly Gln Leu Lys Pro Leu Ser Lys Gln Asp Leu Gly Leu His Ala Tyr
 165 170 175
 Arg Cys Gln Asp Cys Gly Lys Cys Lys Cys Lys Gln Cys Thr Tyr Pro
 180 185 190
 Arg Pro Leu Pro Ser Asp Trp Ile Cys Asp Lys Gln Cys Leu Cys Ser
 195 200 205
 Ala Gln Asn Val Ile Asp Tyr Gly Thr Cys Val Cys Cys Val Lys Gly
 210 215 220
 Leu Phe Tyr His Cys Ser Asn Asp Asp Gln Asp Asn Cys Ala Asp Asn
 225 230 235 240
 Pro Cys Ser Cys Ser Gln Ser His Cys Cys Thr Arg Trp Ser Ala Met
 245 250 255
 Gly Val Met Ser Leu Phe Leu Pro Cys Leu Trp Cys Tyr Leu Pro Ala
 260 265 270
 Lys Gly Cys Leu Lys Leu Cys Gln Gly Cys Tyr Asp Arg Val Asn Arg
 275 280 285
 Pro Gly Cys Arg Cys Lys Asn Ser Asn Thr Val Cys Cys Lys Val Pro
 290 295 300
 Thr Val Pro Pro Arg Asn Phe Gln Lys Pro Thr
 305 310 315
 <210> 146
 <211> 288
 <212> PRT
 <213> Homo sapiens
 <400> 146
 Met Asp Ala Ala Val Thr Asp Asp Phe Gln Gln Ile Leu Pro Ile Gln
 1 5 10 15
 Gln Leu Arg Ser Thr His Ala Ser Asn Asp Tyr Val Gln Arg Pro Pro
 20 25 30

Ala Pro Cys Lys Gln Ala Leu Ser Ser Pro Ser Leu Ile Val Gln Thr 35 40 45
 His Lys Ser Asp Trp Ser Leu Ala Thr Met Pro Thr Ser Leu Pro Arg 50 55 60
 Ser Leu Ser Gln Cys His Gln Leu Gln Pro Leu Pro Gln His Leu Ser 65 70 75 80
 Gln Ser Ser Ile Ala Ser Ser Met Ser His Ser Thr Thr Ala Ser Asp 85 90 95
 Gln Arg Leu Leu Ala Ser Ile Thr Pro Ser Pro Ser Gly Gln Ser Ile 100 105 110
 Ile Arg Thr Gln Pro Gly Ala Gly Val His Pro Lys Ala Asp Gly Ala 115 120 125
 Leu Lys Gly Glu Ala Glu Gln Ser Ala Gly His Pro Ser Glu His Leu 130 135 140
 Phe Ile Cys Glu Glu Cys Gly Arg Cys Lys Cys Val Pro Cys Thr Ala 145 150 155 160
 Ala Arg Pro Leu Pro Ser Cys Trp Leu Cys Asn Gln Arg Cys Leu Cys 165 170 175
 Ser Ala Glu Ser Leu Leu Asp Tyr Gly Thr Cys Leu Cys Cys Val Lys 180 185 190
 Gly Leu Phe Tyr His Cys Ser Thr Asp Asp Glu Asp Asn Cys Ala Asp 195 200 205
 Glu Pro Cys Ser Cys Gly Pro Ser Ser Cys Phe Val Arg Trp Ala Ala 210 215 220
 Met Ser Leu Ile Ser Leu Phe Leu Pro Cys Leu Cys Cys Tyr Leu Pro 225 230 235 240
 Thr Arg Gly Cys Leu His Leu Cys Gln Gln Gly Tyr Asp Ser Leu Arg 245 250 255
 Arg Pro Gly Cys Arg Cys Lys Arg His Thr Asn Thr Val Cys Arg Lys 260 265 270
 Ile Ser Ser Gly Ser Ala Pro Phe Pro Lys Ala Gln Glu Lys Ser Val 275 280 285
 <210> 147
 Met Leu Ser Pro Leu Pro Thr Gly Pro Leu Glu Ala Cys Phe Ser Val 1 5 10 15
 Gln Ser Arg Thr Ser Ser Pro Met Glu Pro Pro Ile Pro Gln Ser Ala 20 25 30
 Pro Leu Thr Pro Asn Ser Val Met Val Gln Pro Leu Leu Asp Ser Arg 285

289

Met Ser His Ser Arg Leu Gln His Pro Leu Thr Ile Leu Pro Ile Asp 35 40 45
 Gln Val Lys Thr Ser His Val Glu Asn Asp Tyr Ile Asp Asn Pro Ser 50 55 60
 Leu Ala Leu Thr Thr Gly Pro Lys Arg Thr Arg Gly Gly Ala Pro Glu 65 70 75 80
 Leu Ala Pro Thr Pro Ala Arg Cys Asp Gln Asp Val Thr His His Trp 85 90 95
 Ile Ser Phe Ser Gly Arg Pro Ser Ser Val Ser Ser Ser Ser Thr 100 105 110
 Ser Ser Asp Gln Arg Leu Leu Asp His Met Ala Pro Pro Val Ala 115 120 125
 Asp Gln Ala Ser Pro Arg Ala Val Arg Ile Gln Pro Lys Val Val His 130 135 140
 Cys Gln Pro Leu Asp Leu Lys Gly Pro Ala Val Pro Glu Leu Asp 145 150 155 160
 Lys His Phe Leu Leu Cys Glu Ala Cys Gly Lys Cys Lys Cys Lys Glu 165 170 175
 Cys Ala Ser Pro Arg Thr Leu Pro Ser Cys Trp Val Cys Asn Gln Glu 180 185 190
 Cys Leu Cys Ser Ala Gln Thr Leu Val Asn Tyr Gly Thr Cys Met Cys 195 200 205
 Leu Val Gln Gly Ile Phe Tyr His Cys Thr Asn Glu Asp Asp Glu Gly 210 215 220
 Ser Cys Ala Asp His Pro Cys Ser Cys Ser Arg Ser Asn Cys Cys Ala 225 230 235 240
 Arg Trp Ser Phe Met Gly Ala Leu Ser Val Val Leu Pro Cys Leu Leu 245 250 255
 Cys Tyr Leu Pro Ala Thr Gly Cys Val Lys Leu Ala Gln Arg Gly Tyr 260 265 270
 Asp Arg Leu Arg Arg Pro Gly Cys Arg Cys Lys His Thr Asn Ser Val 275 280 285 300
 Ile Cys Lys Ala Ala Ser Gly Asp Ala Lys Thr Ser Arg Pro Asp Lys 290 295 300
 Pro Phe 305 310 315 320
 <210> 148
 <211> 333
 <212> PRT
 <213> Homo sapiens
 <400> 148

290

Met Ala Ala Ala Ala Gly Thr Ala Thr Ser Gln Arg Phe Phe Gln
1 5 10 15
Ser Phe Ser Asp Ala Leu Ile Asp Glu Asp Pro Gln Ala Ala Leu Glu
20 25 30
Glu Leu Thr Lys Ala Leu Glu Gln Lys Pro Asp Asp Ala Gln Tyr Tyr
35 40 45
Cys Gln Arg Ala Tyr Cys His Ile Leu Leu Gln Tyr Cys Val Ala
50 55 60
Val Ala Asp Ala Lys Lys Ser Leu Glu Leu Leu Pro Asn Asn Ser Thr
65 70 75 80
Ala Met Leu Arg Lys Gly Ile Cys Glu Tyr His Glu Lys Asn Tyr Ala
85 90 95
Ala Ala Leu Glu Thr Phe Thr Glu Gly Gln Lys Leu Asp Ser Ala Asp
100 105 110
Ala Asn Phe Ser Val Trp Ile Lys Arg Cys Gln Glu Ala Gln Asn Gly
115 120 125
Ser Glu Ser Glu Val Trp Thr His Gln Ser Lys Ile Lys Tyr Asp Trp
130 135 140
Tyr Gln Thr Glu Ser Gln Val Val Ile Thr Leu Met Ile Lys Asn Val
145 150 155 160
Gln Lys Asn Asp Val Asn Val Glu Phe Ser Glu Lys Glu Leu Ser Ala
165 170 175
Leu Val Lys Leu Pro Ser Gly Glu Asp Tyr Asn Leu Lys Leu Glu Leu
180 185 190
Leu His Pro Ile Ile Pro Glu Gln Ser Thr Phe Lys Val Leu Ser Thr
195 200 205
Lys Ile Glu Ile Lys Leu Lys Lys Pro Glu Ala Val Arg Trp Glu Lys
210 215 220
Leu Glu Gly Gln Gly Asp Val Pro Thr Pro Lys Gln Phe Val Ala Asp
225 230 235 240
Val Lys Asn Leu Tyr Pro Ser Ser Ser Pro Tyr Thr Arg Asn Trp Asp
245 250 255
Lys Leu Val Gly Glu Ile Lys Glu Glu Glu Lys Asn Glu Lys Leu Glu
260 265 270
Gly Asp Ala Ala Leu Asn Arg Leu Phe Gln Gln Ile Tyr Ser Asp Gly
275 280 285
Ser Asp Glu Val Lys Arg Ala Met Asn Lys Ser Phe Met Glu Ser Gly
290 295 300
Gly Thr Val Leu Ser Thr Asn Trp Ser Asp Val Gly Lys Arg Lys Val
305 310 315 320
Glu Ile Asn Pro Pro Asp Asp Met Glu Trp Lys Lys Tyr
325 330 335

<210> 149
<211> 362
<212> PRT
<213> Homo sapiens

<400> 149
Ser Leu Phe Cys Ile Ser Leu Asn Arg Leu Pro Leu Ser Pro Gly Pro
1 5 10 15
Ser Thr Leu Val Ser Cys Ala Ala Ser Val Arg Ala Met Ala Thr Glu
20 25 30
Glu Lys Lys Pro Glu Thr Glu Ala Ala Arg Ala Gln Pro Thr Pro Ser
35 40 45
Ser Ser Ala Thr Gln Ser Lys Pro Thr Pro Val Lys Pro Asn Tyr Ala
50 55 60
Leu Lys Phe Thr Leu Ala Gly His Thr Lys Ala Val Ser Ser Val Lys
65 70 75 80
Phe Ser Pro Asn Gly Glu Trp Leu Ala Ser Ser Ser Ala Asp Lys Leu
85 90 95
Ile Lys Ile Trp Gly Ala Tyr Asp Gly Lys Phe Glu Lys Thr Ile Ser
100 105 110
Gly His Lys Leu Gly Ile Ser Asp Val Ala Trp Ser Ser Asp Ser Asn
115 120 125
Leu Leu Val Ser Ala Ser Asp Asp Lys Thr Leu Lys Ile Trp Asp Val
130 135 140
Ser Ser Gly Lys Cys Lys Lys Thr Leu Lys Gly His Ser Asn Tyr Val
145 150 155 160
Phe Cys Asn Phe Asn Pro Gln Ser Asn Leu Ile Val Ser Gly Ser
165 170 175
Phe Asp Glu Ser Val Arg Ile Trp Asp Val Lys Thr Gly Lys Cys Leu
180 185 190
Lys Thr Leu Pro Ala His Ser Asp Pro Val Ser Ala Val His Phe Asn
195 200 205
Arg Asp Gly Ser Leu Ile Val Ser Ser Tyr Asp Gly Leu Cys Arg
210 215 220
Ile Trp Asp Thr Ala Ser Gly Gln Cys Leu Lys Thr Leu Ile Asp Asp
225 230 235 240
Asp Asn Pro Pro Val Ser Phe Val Lys Phe Ser Pro Asn Gly Lys Tyr
245 250 255
Ile Leu Ala Ala Thr Leu Asp Asn Thr Leu Lys Leu Trp Asp Tyr Ser
260 265 270
Lys Gly Lys Cys Leu Lys Thr Tyr Thr Gly His Lys Asn Glu Lys Tyr
275 280 285
Cys Ile Phe Ala Asn Phe Ser Val Thr Gly Gly Lys Trp Ile Val Ser
290 295 300 305 310 315 320 325 330 335

290 295 300
 Gly Ser Glu Asp Asn Leu Val Tyr Ile Trp Asn Leu Gln Thr Lys Glu 320
 305 310 315
 Ile Val Gln Lys Leu Gln Gly His Thr Asp Val Val Ile Ser Thr Ala 335
 325 330
 Cys His Pro Thr Glu Asn Ile Ile Ala Ser Ala Ala Leu Glu Asn Asp 350
 340 345
 Lys Thr Ile Lys Leu Trp Lys Ser Asp Cys 360
 355
 <210> 150
 <211> 514
 <212> PRT
 <213> Homo sapiens
 <400> 150
 Met Ser Ile Ser Ser Asp Glu Val Asn Phe Leu Val Tyr Arg Tyr Leu 15
 1 5 10
 Gln Glu Ser Gly Phe Ser His Ser Ala Phe Thr Phe Gly Ile Glu Ser 30
 20 25
 His Ile Ser Gln Ser Asn Ile Asn Gly Ala Leu Val Pro Pro Ala Ala 45
 35 40
 Leu Ile Ser Ile Ile Gln Lys Gly Leu Gln Tyr Val Glu Ala Glu Val 60
 50 55
 Ser Ile Asn Glu Asp Gly Thr Leu Phe Asp Gly Arg Pro Ile Glu Ser 80
 65 70 75
 Leu Ser Leu Ile Asp Ala Val Met Pro Asp Val Val Gln Thr Arg Gln 95
 85 90
 Gln Ala Tyr Arg Asp Lys Leu Ala Gln Gln Gln Ala Ala Ala Ala Ala 110
 100 105
 Ala Ala Ala Ala Ala Ser Gln Gln Gly Ser Ala Lys Asn Gly Glu 125
 115 120
 Asn Thr Ala Asn Gly Glu Asn Gly Ala His Thr Ile Ala Asn Asn 140
 130 135 140
 His Thr Asp Met Met Glu Val Asp Gly Asp Val Glu Ile Pro Pro Asn 160
 145 150 155
 Lys Ala Val Val Leu Arg Gly His Glu Ser Glu Val Phe Ile Cys Ala 175
 165 170
 Trp Asn Pro Val Ser Asp Leu Leu Ala Ser Gly Ser Gly Asp Ser Thr 190
 180 185
 Ala Arg Ile Trp Asn Leu Ser Glu Asn Ser Thr Ser Gly Ser Thr Gln 205
 195 200
 Leu Val Leu Arg His Cys Ile Arg Glu Gly Gly Gln Asp Val Pro Ser 220
 210 215

293

Asn Lys Asp Val Thr Ser Leu Asp Trp Asn Ser Glu Gly Thr Leu Leu 240
 225 230 235
 Ala Thr Gly Ser Tyr Asp Gly Phe Ala Arg Ile Trp Thr Lys Asp Gly 255
 245 250
 Asn Leu Ala Ser Thr Leu Gly Gln His Lys Gly Pro Ile Phe Ala Leu 270
 260 265
 Lys Trp Asn Lys Lys Gly Asn Phe Ile Leu Ser Ala Gly Val Asp Lys 285
 275 280
 Thr Thr Ile Ile Trp Asp Ala His Thr Gly Glu Ala Lys Gln Gln Phe 300
 290 295
 Pro Phe His Ser Ala Pro Ala Leu Asp Val Asp Trp Gln Ser Asn Asn 320
 305 310 315
 Thr Phe Ala Ser Cys Ser Thr Asp Met Cys Ile His Val Cys Lys Leu 335
 325 330
 Gly Gln Asp Arg Pro Ile Lys Thr Phe Gln Gly His Thr Asn Glu Val 350
 340 345
 Asn Ala Ile Lys Trp Asp Pro Thr Gly Asn Leu Leu Ala Ser Cys Ser 365
 355 360
 Asp Asp Met Thr Leu Lys Ile Trp Ser Met Lys Gln Asp Asn Cys Val 380
 370 375
 His Asp Leu Gln Ala His Asn Lys Glu Ile Tyr Thr Ile Lys Trp Ser 400
 385 390 395
 Pro Thr Gly Pro Gly Thr Asn Asn Pro Asn Ala Asn Leu Met Leu Ala 415
 405 410
 Ser Ala Ser Phe Asp Ser Thr Val Arg Leu Trp Asp Val Asp Arg Gly 430
 420 425
 Ile Cys Ile His Thr Leu Thr Lys His Gln Glu Pro Val Tyr Ser Val 445
 435 440
 Ala Phe Ser Pro Asp Gly Arg Tyr Leu Ala Ser Gly Ser Phe Asp Lys 460
 450 455
 Cys Val His Ile Trp Asn Thr Gln Thr Gly Ala Leu Val His Ser Tyr 480
 465 470 475
 Arg Gly Thr Gly Gly Ile Phe Glu Val Cys Trp Asn Ala Ala Gly Asp 495
 485 490
 Lys Val Gly Ala Ser Ala Ser Asp Gly Ser Val Cys Val Leu Asp Leu 510
 500 505
 Arg Lys

<210> 151
 <211> 619
 <212> PRT
 <213> Homo sapiens

294

<400> 151
Met Ser Val Ala His Met Ser Leu Gln Ala Ala Ala Leu Leu Lys
1 5 10 15
Gly Arg Ser Val Leu Asp Ala Thr Gly Gln Arg Cys Arg Val Val Lys
20 25 30
Arg Ser Phe Ala Phe Pro Ser Phe Leu Gln Asp Val Val Asp Gly
35 40 45
Ala Asp Thr Phe Asp Ser Phe Phe Ser Lys Lys Glu Glu Met Ser Ser
50 55 60
Met Pro Asp Asp Val Phe Glu Ser Pro Pro Leu Ser Ala Ser Tyr Phe
65 70 75 80
Arg Gly Ile Pro His Ser Ala Ser Pro Val Ser Pro Asp Gly Val Gln
85 90 95
Ile Pro Leu Lys Glu Tyr Gly Arg Ala Pro Val Pro Gly Pro Arg Arg
100 105 110
Gly Lys Arg Ile Ala Ser Lys Val Lys His Phe Ala Phe Asp Arg Lys
115 120 125
Lys Arg His Tyr Gly Leu Gly Val Val Gly Asn Trp Leu Asn Arg Ser
130 135 140
Tyr Arg Arg Ser Ile Ser Ser Thr Val Gln Arg Gln Leu Glu Ser Phe
145 150 155 160
Asp Ser His Arg Pro Tyr Phe Thr Tyr Trp Leu Thr Phe Val His Val
165 170 175
Ile Ile Thr Leu Leu Val Ile Cys Thr Tyr Gly Ile Ala Pro Val Gly
180 185 190
Phe Ala Gln His Val Thr Thr Gln Leu Val Leu Arg Asn Lys Gly Val
195 200 205
Tyr Glu Ser Val Lys Tyr Ile Gln Gln Glu Asn Phe Trp Val Gly Pro
210 215 220
Ser Ser Ile Asp Leu Ile His Leu Gly Ala Lys Phe Ser Pro Cys Ile
225 230 235 240
Arg Lys Asp Gly Gln Ile Glu Gln Leu Val Leu Arg Glu Arg Asp Leu
245 250 255
Glu Arg Asp Ser Gly Cys Cys Val Gln Asn Asp His Ser Gly Cys Ile
260 265 270
Gln Thr Gln Arg Lys Asp Cys Ser Glu Thr Leu Ala Thr Phe Val Lys
275 280 285
Trp Gln Asp Asp Thr Gly Pro Pro Met Asp Lys Ser Asp Leu Gly Gln
290 295 300
Lys Arg Thr Ser Gly Ala Val Cys His Gln Asp Pro Arg Thr Cys Glu
305 310 315 320
Glu Pro Ala Ser Ser Gly Ala His Ile Trp Pro Asp Asp Ile Thr Lys

295

325 330 335
Trp Pro Ile Cys Thr Glu Gln Ala Arg Ser Asn His Thr Gly Phe Leu
340 345 350
His Met Asp Cys Glu Ile Lys Gly Arg Pro Cys Cys Ile Gly Thr Lys
355 360 365
Gly Ser Cys Glu Ile Thr Thr Arg Glu Tyr Cys Glu Phe Met His Gly
370 375 380
Tyr Phe His Glu Glu Ala Thr Leu Cys Ser Gln Val His Cys Leu Asp
385 390 395 400
Lys Val Cys Gly Leu Leu Pro Phe Leu Asn Pro Glu Val Pro Asp Gln
405 410 415
Phe Tyr Arg Leu Trp Leu Ser Leu Phe Leu His Ala Gly Val Val His
420 425 430
Cys Leu Val Ser Val Val Phe Gln Met Thr Ile Leu Arg Asp Leu Glu
435 440 445
Lys Leu Ala Gly Trp His Arg Ile Ala Ile Ile Phe Ile Leu Ser Gly
450 455 460
Ile Thr Gly Asn Leu Ala Ser Ala Ile Phe Leu Pro Tyr Arg Ala Glu
465 470 475 480
Val Gly Pro Ala Gly Ser Gln Phe Gly Leu Leu Ala Cys Leu Phe Val
485 490 495
Glu Leu Phe Gln Ser Trp Pro Leu Leu Glu Arg Pro Trp Lys Ala Phe
500 505 510
Leu Asn Leu Ser Ala Ile Val Leu Phe Leu Phe Ile Cys Gly Leu Leu
515 520 525
Pro Trp Ile Asp Asn Ile Ala His Ile Phe Gly Phe Leu Ser Gly Leu
530 535 540
Leu Leu Ala Phe Ala Phe Leu Pro Tyr Ile Thr Phe Gly Thr Ser Asp
545 550 555 560
Lys Tyr Arg Lys Arg Ala Leu Ile Leu Val Ser Leu Leu Ala Phe Ala
565 570 575
Gly Leu Phe Ala Ala Leu Val Leu Trp Leu Tyr Ile Tyr Pro Ile Asn
580 585 590
Trp Pro Trp Ile Glu His Leu Thr Cys Phe Pro Phe Thr Ser Arg Phe
595 600 605
Cys Glu Lys Tyr Glu Leu Asp Gln Val Leu His
610 615
<210> 152
<211> 607
<212> PRT
<213> Homo sapiens
<400> 152

296

Met Glu Ala Pro Ala Ala Gly Leu Phe Leu Leu Leu Leu Gly Thr
 1 5 10 15
 Trp Ala Pro Ala Pro Gly Ser Ala Ser Ser Glu Ala Pro Pro Leu Ile
 20 25 30
 Asn Glu Asp Val Lys Arg Thr Val Asp Leu Ser Ser His Leu Ala Lys
 35 40 45
 Val Thr Ala Glu Val Val Leu Ala His Leu Gly Gly Ser Thr Ser
 50 55 60
 Arg Ala Thr Ser Phe Leu Leu Ala Leu Glu Pro Glu Leu Glu Ala Arg
 65 70 75 80
 Leu Ala His Leu Gly Val Gln Val Lys Gly Glu Asp Glu Glu Glu Asn
 85 90 95
 Asn Leu Glu Val Arg Glu Thr Lys Ile Lys Gly Lys Ser Gly Arg Phe
 100 105 110
 Phe Thr Val Lys Leu Pro Val Ala Leu Asp Pro Gly Ala Lys Ile Ser
 115 120 125
 Val Ile Val Glu Thr Val Tyr Thr His Val Leu His Pro Tyr Pro Thr
 130 135 140
 Gln Ile Thr Gln Ser Glu Lys Gln Phe Val Val Phe Glu Gly Asn His
 145 150 155 160
 Tyr Phe Tyr Ser Pro Tyr Pro Thr Lys Thr Gln Thr Met Arg Val Lys
 165 170 175
 Leu Ala Ser Arg Asn Val Glu Ser Tyr Thr Lys Leu Gly Asn Pro Thr
 180 185 190
 Arg Ser Glu Asp Leu Leu Asp Tyr Gly Pro Phe Arg Asp Val Pro Ala
 195 200 205
 Tyr Ser Gln Asp Thr Phe Lys Val His Tyr Glu Asn Asn Ser Pro Phe
 210 215 220
 Leu Thr Ile Thr Ser Met Thr Arg Val Ile Glu Val Ser His Trp Gly
 225 230 235 240
 Asn Ile Ala Val Glu Glu Asn Val Asp Leu Lys His Thr Gly Ala Val
 245 250 255
 Leu Lys Gly Pro Phe Ser Arg Tyr Asp Tyr Gln Arg Gln Pro Asp Ser
 260 265 270
 Gly Ile Ser Ser Ile Arg Ser Phe Lys Thr Ile Leu Pro Ala Ala Ala
 275 280 285
 Gln Asp Val Tyr Tyr Arg Asp Glu Ile Gly Asn Val Ser Thr Ser His
 290 295 300
 Leu Leu Ile Leu Asp Asp Ser Val Glu Met Glu Ile Arg Pro Arg Phe
 305 310 315 320
 Pro Leu Phe Gly Gly Trp Lys Thr His Tyr Ile Val Gly Tyr Asn Leu
 325 330 335

Pro Ser Tyr Glu Tyr Leu Tyr Asn Leu Gly Asp Gln Tyr Ala Leu Lys 340 345 350
Met Arg Phe Val Asp Phe His Val Phe Asp Glu Gln Val Ile Asp Ser Leu 355 360 365
Thr Val Lys Ile Ile Leu Pro Glu Gly Ala Lys Asn Ile Glu Ile Asp 370 375 380
Ser Pro Tyr Glu Ile Ser Arg Ala Pro Asp Glu Leu His Tyr Thr Tyr 385 390 395 400
Leu Asp Thr Phe Gly Arg Pro Val Ile Val Ala Tyr Lys Lys Asn Leu 405 410 415
Val Glu Gln His Ile Gln Asp Ile Val Val His Tyr Thr Phe Asn Lys 420 425 430
Val Leu Met Leu Gln Glu Pro Leu Leu Val Val Ala Phe Tyr Ile 435 440 445
Leu Phe Phe Thr Val Ile Ile Tyr Val Arg Leu Asp Phe Ser Ile Thr 450 455 460
Lys Asp Pro Ala Ala Glu Ala Arg Met Lys Val Ala Cys Ile Thr Glu 465 470 475 480
Gln Val Leu Thr Leu Val Asn Lys Arg Ile Gly Leu Tyr Arg His Phe 485 490 495
Asp Glu Thr Val Asn Arg Tyr Lys Gln Ser Arg Asp Ile Ser Thr Leu 500 505 510
Asn Ser Gly Lys Lys Ser Leu Glu Thr Glu His Lys Ala Leu Thr Ser 515 520 525
Glu Ile Ala Leu Leu Gln Ser Arg Leu Lys Thr Glu Gly Ser Asp Leu 530 535 540
Cys Asp Arg Val Ser Glu Met Gln Lys Leu Asp Ala Gln Val Lys Glu 545 550 555 560
Leu Val Leu Lys Ser Ala Val Glu Ala Glu Arg Leu Val Ala Gly Lys 565 570 575
Leu Lys Lys Asp Thr Tyr Ile Glu Asn Glu Lys Leu Ile Ser Gly Lys 580 585 590
Arg Gln Glu Leu Val Thr Lys Ile Asp His Ile Leu Asp Ala Leu 595 600 605
<210> 133
<211> 601
<212> PRT
<213> Homo sapiens
<400> 133
Arg Trp Leu Arg Arg Ala Pro Ala Asp Met Ala Ala Val Ala Ala 1 5 10 15
Ala Leu Ala Arg Leu Leu Ala Ala Phe Leu Leu Leu Ala Ala Gln Val

298

Ala Cys Glu Tyr Gly Met Val His Val Val Ser Gln Ala Gly Gly Pro 35 40 45 30
Glu Gly Lys Asp Tyr Cys Ile Leu Tyr Asn Pro Gln Trp Ala His Leu 50 55 60
Pro His Asp Leu Ser Lys Ala Ser Phe Leu Gln Leu Arg Asn Trp Thr 65 70 75 80
Ala Ser Leu Leu Cys Ser Ala Ala Asp Leu Pro Ala Arg Gly Phe Ser 85 90 95
Asn Gln Ile Pro Leu Val Ala Arg Gly Asn Cys Thr Phe Tyr Glu Lys 100 105 110
Val Arg Leu Ala Gln Gly Ser Gly Ala Arg Gly Leu Leu Ile Val Ser 115 120 125
Arg Glu Arg Leu Val Pro Gly Gly Asn Lys Thr Gln Tyr Asp Glu 130 135 140
Ile Gly Ile Pro Val Ala Leu Leu Ser Tyr Lys Asp Met Leu Asp Ile 145 150 155 160
Phe Thr Arg Phe Gly Arg Thr Val Arg Ala Ala Leu Tyr Ala Pro Lys 165 170 175
Glu Pro Val Leu Asp Tyr Asn Met Val Ile Ile Phe Ile Met Ala Val 180 185 190
Gly Thr Val Ala Ile Gly Gly Tyr Trp Ala Gly Ser Arg Asp Val Lys 195 200 205
Lys Arg Tyr Met Lys His Lys Arg Asp Asp Gly Pro Glu Lys Gln Glu 210 215 220
Asp Glu Ala Val Asp Val Thr Pro Val Met Thr Cys Val Phe Val Val 225 230 235 240
Met Cys Cys Ser Met Leu Val Leu Leu Tyr Tyr Phe Tyr Asp Leu Leu 245 250 255
Val Tyr Val Val Ile Gly Ile Phe Cys Leu Ala Ser Ala Thr Gly Leu 260 265 270
Tyr Ser Cys Leu Ala Pro Cys Val Arg Arg Leu Pro Phe Gly Lys Cys 275 280 285
Arg Ile Pro Asn Asn Ser Leu Pro Tyr Phe His Lys Arg Pro Gln Ala 290 295 300
Arg Met Leu Leu Leu Ala Leu Phe Cys Val Ala Val Ser Val Val Trp 305 310 315 320
Gly Val Phe Arg Asn Glu Asp Gln Trp Ala Trp Val Leu Gln Asp Ala 325 330 335
Leu Gly Ile Ala Phe Cys Leu Tyr Met Leu Lys Thr Ile Arg Leu Pro 340 345 350

299

Thr Phe Lys Ala Cys Thr Leu Leu Leu Val Leu Phe Leu Tyr Asp 365
 Ile Phe Phe Val Phe Ile Thr Pro Phe Leu Thr Lys Ser Gly Ser Ser 370
 Ile Met Val Glu Val Ala Thr Gly Pro Ser Asp Ser Ala Thr Arg Glu 385
 Lys Leu Pro Met Val Leu Lys Val Pro Arg Leu Asn Ser Ser Pro Leu 405
 Ala Leu Cys Asp Arg Pro Phe Ser Leu Leu Gly Phe Gly Asp Ile Leu 420
 Val Pro Gly Leu Leu Val Ala Tyr Cys His Arg Phe Asp Ile Gln Val 435
 Gln Ser Ser Arg Val Tyr Phe Val Ala Cys Thr Ile Ala Tyr Gly Val 450
 Gly Leu Leu Val Thr Phe Val Ala Leu Ala Leu Met Gln Arg Gly Gln 465
 Pro Ala Leu Leu Tyr Leu Val Pro Cys Thr Leu Val Thr Ser Cys Ala 485
 Val Ala Leu Trp Arg Arg Glu Leu Gly Val Phe Trp Thr Gly Ser Gly 500
 Phe Ala Lys Val Leu Pro Pro Ser Pro Trp Ala Pro Ala Pro Ala Asp 515
 Gly Pro Gln Pro Pro Lys Asp Ser Ala Thr Pro Leu Ser Pro Gln Pro 530
 Pro Ser Glu Glu Pro Ala Thr Ser Pro Trp Pro Ala Glu Gln Ser Pro 545
 Lys Ser Arg Thr Ser Glu Glu Met Gly Ala Gly Ala Pro Met Arg Glu 565
 Pro Gly Ser Pro Ala Glu Ser Glu Gly Arg Asp Gln Ala Gln Pro Ser 580
 Pro Val Thr Gln Pro Gly Ala Ser Ala 600
 <210> 154
 <211> 377
 <212> PRT
 <213> Homo sapiens
 <400> 154
 Met Asp Ser Ala Leu Ser Asp Pro His Asn Gly Ser Ala Glu Ala Gly 1
 Gly Pro Thr Asn Ser Thr Thr Arg Pro Pro Ser Thr Pro Glu Gly Ile 20
 Ala Leu Ala Tyr Gly Ser Leu Leu Met Ala Leu Leu Pro Ile Phe 35

300

Phe Gly Ala Leu Arg Ser Val Arg Cys Ala Arg Gly Lys Asn Ala Ser 50
 Asp Met Pro Glu Thr Ile Thr Ser Arg Asp Ala Ala Arg Phe Pro Ile 65
 Ile Ala Ser Cys Thr Leu Leu Gly Leu Tyr Leu Phe Phe Lys Ile Phe 85
 Ser Gln Glu Tyr Ile Asn Leu Leu Ser Met Tyr Phe Phe Val Leu 100
 Gly Ile Leu Ala Leu Ser His Thr Ile Ser Pro Phe Met Asn Lys Phe 115
 Phe Pro Ala Ser Phe Pro Asn Arg Gln Tyr Gln Leu Leu Phe Thr Gln 130
 Gly Ser Gly Glu Asn Lys Glu Glu Ile Ile Asn Tyr Glu Phe Asp Thr 145
 Lys Asp Leu Val Cys Leu Gly Leu Ser Ser Ile Val Gly Val Trp Tyr 165
 Leu Leu Arg Lys His Trp Ile Ala Asn Asn Leu Phe Gly Leu Ala Phe 180
 Ser Leu Asn Gly Val Glu Leu Leu His Leu Asn Asn Val Ser Thr Gly 195
 Cys Ile Leu Leu Gly Gly Leu Phe Ile Tyr Asp Val Phe Trp Val Phe 210
 Gly Thr Asn Val Met Val Thr Val Ala Lys Ser Phe Glu Ala Pro Ile 225
 Lys Leu Val Phe Pro Gln Asp Leu Leu Glu Lys Gly Leu Glu Ala Asn 245
 Asn Phe Ala Met Leu Gly Leu Gly Asp Val Val Ile Pro Gly Ile Phe 260
 Ile Ala Leu Leu Leu Arg Phe Asp Ile Ser Leu Lys Lys Asn Thr His 275
 Thr Tyr Phe Tyr Thr Ser Phe Ala Ala Tyr Ile Phe Gly Leu Gly Leu 290
 Thr Ile Phe Ile Met His Ile Phe Lys His Ala Gln Pro Ala Leu Leu 305
 Tyr Leu Val Pro Ala Cys Ile Gly Phe Pro Val Leu Val Ala Leu Ala 325
 Lys Gly Glu Val Thr Glu Met Phe Ser Tyr Glu Glu Ser Asn Pro Lys 340
 Asp Pro Ala Ala Val Thr Glu Ser Lys Glu Gly Thr Glu Ala Ser Ala 355
 Ser Lys Gly Leu Glu Lys Lys Glu Lys

301

370 375
 <210> 155
 <211> 743
 <212> PRT
 <213> Homo sapiens
 <400> 155
 1 Met Ala Val Ala Val Arg Thr Leu Gln Gln Leu Glu Lys Ala Lys 15
 10
 Glu Ser Leu Lys Asn Val Asp Glu Asn Ile Arg Lys Leu Thr Gly Arg 30
 20 25
 Asp Pro Asn Asp Val Arg Pro Ile Gln Ala Arg Leu Leu Ala Leu Ser 45
 35
 Gly Pro Gly Gly Arg Gly Arg Gly Ser Leu Leu Leu Arg Arg Gly 60
 50 55
 Phe Ser Asp Ser Gly Gly Pro Pro Ala Lys Gln Arg Asp Leu Glu Gly 80
 65 70 75
 Ala Val Ser Arg Leu Gly Gly Arg Arg Thr Arg Arg Glu Ser Arg 95
 85 90
 Gln Glu Ser Asp Pro Glu Asp Asp Val Lys Lys Pro Ala Leu Gln 110
 100 105
 Ser Ser Val Val Ala Thr Ser Lys Glu Arg Thr Arg Arg Asp Leu Ile 120
 115 125
 Gln Asp Gln Asn Met Asp Glu Lys Gly Lys Gln Arg Asn Arg Arg Ile 140
 130 135
 Phe Gly Leu Leu Met Gly Thr Leu Gln Lys Phe Lys Gln Glu Ser Thr 160
 145 150 155
 Val Ala Thr Glu Arg Gln Asn Arg Arg Gln Glu Ile Glu Gln Lys Leu 175
 165 170
 Glu Val Gln Ala Glu Glu Arg Lys Gln Val Glu Asn Glu Arg Arg 190
 180 185
 Glu Leu Phe Glu Glu Arg Arg Ala Lys Gln Thr Glu Leu Arg Leu Leu 205
 195 200
 Glu Gln Lys Val Glu Leu Ala Gln Leu Gln Glu Glu Trp Asn Glu His 220
 210 215
 Asn Ala Lys Ile Ile Lys Tyr Ile Arg Thr Lys Thr Lys Pro His Leu 240
 225 230 235
 Phe Tyr Ile Pro Gly Arg Met Cys Pro Ala Thr Gln Lys Leu Ile Glu 255
 245 250
 Glu Ser Gln Arg Lys Met Asn Ala Leu Phe Asp Gly Arg Arg Ile Glu 270
 260 265
 Phe Ala Glu Gln Ile Asn Lys Met Glu Ala Arg Pro Arg Arg Gln Ser 285
 275 280

302

Met Lys Glu Lys Glu His Gln Val Val Arg Asn Glu Glu His Lys Ala 300
 290 295
 Glu Gln Glu Glu Gly Lys Val Ala Gln Arg Glu Glu Leu Val Glu 320
 305 310 315
 Thr Gly Asn Gln His Asn Asp Val Glu Ile Glu Glu Ala Gly Glu Glu 335
 320 325
 Glu Glu Lys Glu Ile Gly Ile Val His Ser Asp Ala Glu Lys Glu Gln 350
 340 345
 Glu Glu Glu Glu Gln Lys Gln Met Glu Val Lys Met Glu Glu Glu 365
 355 360
 Thr Glu Val Arg Glu Ser Glu Lys Gln Gln Asp Ser Gln Pro Glu Glu 380
 370 375
 Val Met Asp Val Leu Glu Met Val Glu Asn Val Lys His Val Ile Ala 400
 385 390 395
 Asp Gln Glu Val Met Glu Thr Asn Arg Val Glu Ser Val Glu Pro Ser 415
 405 410
 Glu Asn Glu Ala Ser Lys Glu Leu Glu Pro Glu Met Glu Phe Glu Ile 430
 420 425
 Glu Pro Asp Lys Glu Cys Lys Ser Leu Ser Pro Gly Lys Glu Asn Val 445
 435 440
 Ser Ala Leu Asp Met Glu Lys Glu Ser Asp Glu Lys Glu Glu Lys Glu 460
 450 455
 Ser Glu Pro Gln Pro Glu Pro Val Ala Gln Pro Gln Ala Gln Ser Gln 480
 465 470 475
 Pro Gln Leu Gln Leu Gln Ser Gln Ser Glu Pro Gln Pro Gln Leu Gln 495
 485 490
 Pro Glu Pro Ala Gln Pro Gln Leu Gln Ser Gln Pro Gln Leu Gln Leu 510
 500 505
 Gln Ser Gln Cys His Ala Val Leu Gln Ser His Pro Pro Ser Gln Pro 525
 515 520
 Glu Asp Leu Ser Leu Ala Val Leu Gln Pro Thr Pro Gln Val Thr Gln 540
 530 535
 Glu His Gly His Phe Leu Pro Glu Arg Lys Asp Phe Pro Val Glu Ser 560
 545 550 555
 Val Lys Leu Thr Glu Val Pro Val Asp Pro Val Leu Thr Val His Pro 575
 565 570
 Glu Ser Glu Ser Glu Thr Asn Thr Arg Ser Arg Ser Arg Gly Arg Thr 590
 580 585
 Arg Asn Arg Thr Thr Lys Ser Arg Ser Arg Ser Ser Ser Ser Ser 605
 595 600
 Ser Ser Ser Ser Thr Ser Ser Ser Gly Ser Ser Ser Ser Ser 620
 610 615

303

Gly Ser Ser Ser Arg Ser Ser Ser Ser Ser Ser Thr Ser
 625 630 635 640
 Gly Ser Ser Ser Arg Asp Ser Ser Ser Thr Ser Ser Ser Ser Glu
 645 650 655
 Ser Arg Ser Ser Arg Ser Arg Gly Arg Gly His Asn Arg Asp Arg Lys His
 660 665 670
 Arg Arg Ser Val Asp Arg Lys Arg Arg Asp Thr Ser Gly Leu Glu Arg
 675 680 685
 Ser His Lys Ser Ser Lys Gly Ser Ser Arg Asp Thr Lys Gly Ser
 690 695 700
 Lys Asp Lys Asn Ser Arg Ser Asp Arg Lys Arg Ser Ile Ser Glu Ser
 705 710 715 720
 Ser Arg Ser Gly Lys Arg Ser Ser Arg Ser Glu Arg Asp Arg Lys Ser
 725 730 735
 Asp Arg Lys Asp Lys Arg Arg
 740
 <210> 156
 <211> 442
 <212> PRT
 <213> Homo sapiens
 <400> 156
 Met Ala Ser Val Val Leu Pro Ser Gly Ser Gln Cys Ala Ala Ala
 1 5 10 15
 Ala Ala Ala Pro Gly Leu Arg Leu Arg Leu Leu Leu Leu
 20 25 30
 Phe Ser Ala Ala Ala Leu Ile Pro Thr Gly Asp Gly Gln Asn Leu Phe
 35 40 45
 Thr Lys Asp Val Thr Val Ile Glu Gly Glu Val Ala Thr Ile Ser Cys
 50 55 60
 Gln Val Asn Lys Ser Asp Asp Ser Val Ile Gln Leu Leu Asn Pro Asn
 65 70 75 80
 Arg Gln Thr Ile Tyr Phe Arg Asp Phe Arg Pro Leu Lys Asp Ser Arg
 85 90 95
 Phe Gln Leu Leu Asn Phe Ser Ser Ser Glu Leu Lys Val Ser Leu Thr
 100 105 110
 Asn Val Ser Ile Ser Asp Glu Gly Arg Tyr Phe Cys Gln Leu Tyr Thr
 115 120 125
 Asp Pro Gln Glu Ser Tyr Thr Thr Ile Thr Val Leu Val Pro Pro
 130 135 140
 Arg Asn Leu Met Ile Asp Ile Gln Arg Asp Thr Ala Val Glu Gly Glu
 145 150 155 160
 Glu Ile Glu Val Asn Cys Thr Ala Met Ala Ser Lys Pro Ala Thr Thr

165 170 175
 Ile Arg Trp Phe Lys Gly Asn Thr Glu Leu Lys Gly Lys Ser Glu Val
 180 185 190
 Glu Glu Trp Ser Asp Met Tyr Thr Val Thr Ser Gln Leu Met Leu Lys
 195 200 205
 Val His Lys Glu Asp Asp Gly Val Pro Val Ile Cys Gln Val Glu His
 210 215 220
 Pro Ala Val Thr Gly Asn Leu Gln Thr Gln Arg Tyr Leu Glu Val Gln
 225 230 235 240
 Tyr Lys Pro Gln Val His Ile Gln Met Thr Tyr Pro Leu Gln Gly Leu
 245 250 255
 Thr Arg Glu Gly Asp Ala Leu Glu Leu Thr Cys Glu Ala Ile Gly Lys
 260 265 270
 Pro Gln Pro Val Met Val Thr Trp Val Arg Val Asp Asp Glu Met Pro
 275 280 285
 Gln His Ala Val Leu Ser Gly Pro Asn Leu Phe Ile Asn Asn Leu Asn
 290 295 300
 Lys Thr Asp Asn Gly Thr Tyr Arg Cys Glu Ala Ser Asn Ile Val Gly
 305 310 315 320
 Lys Ala His Ser Asp Tyr Met Leu Tyr Val Tyr Asp Pro Pro Thr Thr
 325 330 335
 Ile Pro Pro Pro Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr
 340 345 350
 Thr Ile Leu Thr Ile Ile Thr Asp Ser Arg Ala Gly Glu Glu Gly Ser
 355 360 365
 Ile Arg Ala Val Asp His Ala Val Ile Gly Gly Val Val Ala Val Val
 370 375 380
 Val Phe Ala Met Leu Cys Leu Leu Ile Ile Leu Gly Arg Tyr Phe Ala
 385 390 395 400
 Arg His Lys Gly Thr Tyr Phe Thr His Glu Ala Lys Gly Ala Asp Asp
 405 410 415
 Ala Ala Asp Ala Asp Thr Ala Ile Ile Asn Ala Glu Gly Gly Gln Asn
 420 425 430
 Asn Ser Glu Glu Lys Lys Glu Tyr Phe Ile
 435 440
 <210> 157
 <211> 1241
 <212> PRT
 <213> Homo sapiens
 <400> 157
 Met Ala Leu Gly Thr Thr Leu Arg Ala Ser Leu Leu Leu Gly Leu
 1 5 10 15

Leu Thr Glu Gly Leu Ala Gln Leu Ala Ile Pro Ala Ser Val Pro Arg 20 25 30
 Gly Phe Trp Ala Leu Pro Glu Asn Leu Thr Val Val Glu Gly Ala Ser 35 40 45
 Val Glu Leu Arg Cys Gly Val Ser Thr Pro Gly Ser Ala Val Gln Trp 50 55 60
 Ala Lys Asp Gly Leu Leu Leu Gly Pro Asp Pro Arg Ile Pro Gly Phe 65 70 75 80
 Pro Arg Tyr Arg Leu Glu Gly Asp Pro Ala Arg Gly Glu Phe His Leu 85 90 95
 His Ile Glu Ala Cys Asp Leu Ser Asp Asp Ala Glu Tyr Glu Cys Gln 100 105 110
 Val Gly Arg Ser Glu Met Gly Pro Glu Leu Val Ser Pro Arg Val Ile 115 120 125
 Leu Ser Ile Leu Val Pro Pro Lys Leu Leu Leu Thr Pro Glu Ala 130 135 140
 Gly Thr Met Val Thr Trp Val Ala Gly Gln Glu Tyr Val Val Asn Cys 145 150 155 160
 Val Ser Gly Asp Ala Lys Pro Ala Pro Asp Ile Thr Ile Leu Leu Ser 165 170 175
 Gly Gln Thr Ile Ser Asp Ile Ser Ala Asn Val Asn Glu Gly Ser Gln 180 185 190
 Gln Lys Leu Phe Thr Val Glu Ala Thr Ala Arg Val Thr Pro Arg Ser 195 200 205
 Ser Asp Asn Arg Gln Leu Leu Val Cys Glu Ala Ser Ser Pro Ala Leu 210 215 220
 Glu Ala Pro Ile Lys Ala Ser Phe Thr Val Asn Val Leu Phe Pro Pro 225 230 235 240
 Gly Pro Pro Val Ile Glu Trp Pro Gly Leu Asp Glu Gly His Val Arg 245 250 255
 Ala Gly Gln Ser Leu Glu Leu Pro Cys Val Ala Arg Gly Gly Asn Pro 260 265 270
 Leu Ala Thr Leu Gln Trp Leu Lys Asn Gly Gln Pro Val Ser Thr Ala 275 280 285
 Trp Gly Thr Glu His Thr Gln Ala Val Ala Arg Ser Val Leu Val Met 290 295 300
 Thr Val Arg Pro Glu Asp His Gly Ala Gln Leu Ser Cys Glu Ala His 305 310 315 320
 Asn Ser Val Ser Ala Gly Thr Gln Glu His Gly Ile Thr Leu Gln Val 325 330 335
 Thr Phe Pro Pro Ser Ala Ile Ile Ile Leu Gly Ser Ala Ser Gln Thr 340 345 350

306

Glu Asn Lys Asn Val Thr Leu Ser Cys Val Ser Lys Ser Ser Arg Pro 355 360 365
 Arg Val Leu Leu Arg Trp Trp Leu Gly Trp Arg Gln Leu Leu Pro Met 370 375 380
 Glu Glu Thr Val Met Asp Gly Leu His Gly Gly His Ile Ser Met Ser 385 390 395 400
 Asn Leu Thr Phe Leu Ala Arg Arg Glu Asp Asn Gly Leu Thr Leu Thr 405 410 415
 Cys Glu Ala Phe Ser Glu Ala Phe Thr Lys Glu Thr Phe Lys Lys Ser 420 425 430
 Leu Ile Leu Asn Val Lys Tyr Pro Ala Gln Lys Leu Trp Ile Glu Gly 435 440 445
 Pro Pro Glu Gly Gln Lys Leu Arg Ala Gly Thr Arg Val Arg Leu Val 450 455 460
 Cys Leu Ala Ile Gly Gly Asn Pro Glu Pro Ser Leu Met Trp Tyr Lys 465 470 475 480
 Asp Ser Arg Thr Val Thr Glu Ser Arg Leu Pro Gln Glu Ser Arg Arg 485 490 495
 Val His Leu Gly Ser Val Glu Lys Ser Gly Ser Thr Phe Ser Arg Glu 500 505 510
 Leu Val Leu Val Thr Gly Pro Ser Asp Asn Gln Ala Lys Phe Thr Cys 515 520 525
 Lys Ala Gly Gln Leu Ser Ala Ser Thr Gln Leu Ala Val Gln Phe Pro 530 535 540
 Pro Thr Asn Val Thr Ile Leu Ala Asn Ala Ser Ala Leu Arg Pro Gly 545 550 555 560
 Asp Ala Leu Asn Leu Thr Cys Val Ser Val Ser Ser Asn Pro Pro Val 565 570 575
 Asn Leu Ser Trp Asp Lys Glu Gly Glu Arg Leu Glu Gly Val Ala Ala 580 585 590
 Pro Pro Arg Arg Ala Pro Phe Lys Gly Ser Ala Ala Ala Arg Ser Val 595 600 605
 Leu Leu Gln Val Ser Ser Arg Asp His Gly Gln Arg Val Thr Cys Arg 610 615 620
 Ala His Ser Ala Glu Leu Arg Glu Thr Val Ser Ser Phe Tyr Arg Leu 625 630 635 640
 Asn Val Leu Tyr Arg Pro Glu Phe Leu Gly Glu Gln Val Leu Val Val 645 650 655
 Thr Ala Val Glu Gln Gly Glu Ala Leu Leu Pro Val Ser Val Ser Ala 660 665 670
 Asn Pro Ala Pro Glu Ala Phe Asn Trp Thr Phe Arg Gly Tyr Arg Leu

307

675 680 685
 Ser Pro Ala Gly Gly Pro Arg His Arg Ile Leu Ser Ser Gly Ala Leu
 690 700
 His Leu Trp Asn Val Thr Arg Ala Asp Asp Gly Leu Tyr Gln Leu His
 705 710 715 720
 Cys Gln Asn Ser Gly Gly Thr Ala Glu Ala Arg Leu Arg Leu Asp Val
 725 730 735
 His Tyr Ala Pro Thr Ile Arg Ala Leu Gln Asp Pro Thr Glu Val Asn
 740 745 750
 Val Gly Gly Ser Val Asp Ile Val Cys Thr Val Asp Ala Asn Pro Ile
 755 760 765
 Leu Pro Gly Met Phe Asn Trp Glu Arg Leu Gly Glu Asp Glu Glu Asp
 770 775 780
 Gln Ser Leu Asp Asp Met Glu Lys Ile Ser Arg Gly Pro Thr Gly Arg
 785 790 795 800
 Leu Arg Ile His His Ala Lys Leu Ala Gln Ala Gly Ala Tyr Gln Cys
 805 810 815
 Ile Val Asp Asn Gly Val Ala Pro Pro Ala Arg Arg Leu Leu Arg Leu
 820 825 830
 Val Val Arg Phe Ala Pro Gln Val Glu His Pro Thr Pro Leu Thr Lys
 835 840 845
 Val Ala Ala Ala Gly Asp Ser Thr Ser Ala Thr Leu His Cys Arg
 850 855 860
 Ala Arg Gly Val Pro Asn Ile Val Phe Thr Trp Thr Lys Asn Gly Val
 865 870 875 880
 Pro Leu Asp Leu Gln Asp Pro Arg Tyr Thr Glu His Thr Tyr His Gln
 885 890 895
 Gly Gly Val His Ser Ser Leu Leu Thr Ile Ala Asn Val Ser Ala Ala
 900 905 910
 Gln Asp Tyr Ala Leu Phe Thr Cys Thr Ala Thr Asn Ala Leu Gly Ser
 915 920 925
 Asp Gln Thr Asn Ile Gln Leu Val Ser Ile Ser Arg Pro Asp Pro Pro
 930 935 940
 Ser Gly Leu Lys Val Val Ser Leu Thr Pro His Ser Val Gly Leu Glu
 945 950 955 960
 Trp Lys Pro Gly Phe Asp Gly Gly Leu Pro Gln Arg Phe Cys Ile Arg
 965 970 975
 Tyr Glu Ala Leu Gly Thr Pro Gly Phe His Tyr Val Asp Val Val Pro
 980 985 990
 Pro Gln Ala Thr Thr Phe Thr Leu Thr Gly Leu Gln Pro Ser Thr Arg
 995 1000 1005

Tyr Arg Val Trp Leu Leu Ala Ser Asn Ala Leu Gly Asp Ser Gly
 1010 1015 1020
 Leu Ala Asp Lys Gly Thr Gln Leu Pro Ile Thr Thr Pro Gly Leu
 1025 1030 1035
 His Gln Pro Ser Gly Glu Pro Glu Asp Gln Leu Pro Thr Glu Pro
 1040 1045 1050
 Pro Ser Gly Pro Ser Gly Leu Pro Leu Leu Pro Val Leu Phe Ala
 1055 1060 1065
 Leu Gly Gly Leu Leu Leu Leu Ser Asn Ala Ser Cys Val Gly Gly
 1070 1075 1080
 Val Leu Trp Gln Arg Arg Leu Arg Arg Leu Ala Glu Gly Ile Ser
 1085 1090 1095
 Glu Lys Thr Glu Ala Gly Ser Glu Glu Asp Arg Val Arg Asn Glu
 1100 1105 1110
 Tyr Glu Glu Ser Gln Trp Thr Gly Glu Arg Asp Thr Gln Ser Ser
 1115 1120 1125
 Thr Val Ser Thr Thr Glu Ala Glu Pro Tyr Tyr Arg Ser Leu Arg
 1130 1135 1140
 Asp Phe Ser Pro Gln Leu Pro Pro Thr Gln Glu Glu Val Ser Tyr
 1145 1150 1155
 Ser Arg Gly Phe Thr Gly Glu Asp Glu Asp Met Ala Phe Pro Gly
 1160 1165 1170
 His Leu Tyr Asp Glu Val Glu Arg Thr Tyr Pro Pro Ser Gly Ala
 1175 1180 1185
 Trp Gly Pro Leu Tyr Asp Glu Val Gln Met Gly Pro Trp Asp Leu
 1190 1195 1200
 His Trp Pro Glu Asp Thr Tyr Gln Asp Pro Arg Gly Ile Tyr Asp
 1205 1210 1215
 Gln Val Ala Gly Asp Leu Asp Thr Leu Glu Pro Asp Ser Leu Pro
 1220 1225 1230
 Phe Glu Leu Arg Gly His Leu Val
 1235 1240
 <210> 158
 <211> 372
 <212> PRT
 <213> Homo sapiens
 <400> 158
 Met Asp Val Leu Ser Pro Leu Ser Phe Ile Lys Val Ser His Val Arg
 1 5 10 15
 Met Gln Gly Ile Leu Leu Leu Val Phe Ala Lys Tyr Gln His Leu Pro
 20 25 30
 Tyr Ile Gln Ile Leu Ser Thr Lys Ser Thr Pro Thr Gly Leu Phe Gly
 35 40 45

Tyr Trp Gly Asn Lys Gly Gly Val Asn Ile Cys Leu Lys Leu Tyr Gly
 50 55 60
 Tyr Tyr Val Ser Ile Ile Asn Cys His Leu Pro Pro His Ile Ser Asn
 65 70 75 80
 Asn Tyr Gln Arg Leu Gln His Phe Asp Arg Ile Leu Gln Met Gln Asn
 85 90 95
 Cys Glu Gly Arg Asp Ile Pro Asn Ile Leu Asp His Asp Leu Ile Ile
 100 105 110
 Trp Phe Gly Asp Met Asn Phe Arg Ile Glu Asp Phe Gly Leu His Phe
 115 120 125
 Val Arg Glu Ser Ile Lys Asn Arg Cys Tyr Gly Leu Trp Glu Lys
 130 135 140
 Asp Gln Leu Ser Ile Ala Lys Lys His Asp Pro Leu Leu Arg Glu Phe
 145 150 155 160
 Gln Glu Gly Arg Leu Leu Phe Pro Pro Thr Tyr Lys Phe Asp Arg Asn
 165 170 175
 Ser Asn Asp Tyr Asp Thr Ser Glu Lys Lys Arg Lys Pro Ala Trp Thr
 180 185 190
 Asp Arg Ile Leu Trp Arg Leu Lys Arg Gln Pro Cys Ala Gly Pro Asp
 195 200 205
 Thr Pro Ile Pro Pro Ala Ser His Phe Ser Leu Ser Leu Arg Gly Tyr
 210 215 220
 Ser Ser His Met Thr Tyr Gly Ile Ser Asp His Lys Lys Pro Val Ser Gly
 225 230 235 240
 Thr Phe Asp Leu Glu Leu Lys Pro Leu Val Ser Ala Pro Leu Ile Val
 245 250 255
 Leu Met Pro Glu Asp Leu Trp Thr Val Glu Asn Asp Met Met Val Ser
 260 265 270
 Tyr Ser Ser Thr Ser Asp Phe Pro Ser Ser Pro Trp Asp Trp Ile Gly
 275 280 285
 Leu Tyr Lys Val Gly Leu Arg Asp Val Asn Asp Tyr Val Ser Tyr Ala
 290 295 300
 Trp Val Gly Asp Ser Lys Val Ser Cys Ser Asp Asn Leu Asn Gln Val
 305 310 315 320
 Tyr Ile Asp Ile Ser Asn Ile Pro Thr Thr Glu Asp Glu Phe Leu Leu
 325 330 335
 Cys Tyr Tyr Arg Asn Ser Leu Arg Ser Val Val Gly Ile Arg Arg Pro
 340 345 350
 Phe Gln Ile Pro Pro Gly Ser Leu Arg Glu Asp Pro Leu Gly Glu Ala
 355 360 365
 Gln Pro Gln Ile

310

370

<210> 159
 <211> 1709
 <212> PRT
 <213> Homo sapiens
 <400> 159
 Met Asn Gly His Ser Asp Glu Glu Ser Val Arg Asn Ser Ser Gly Glu
 1 5 10 15
 Ser Ser Gln Ser Ser Asp Asp Ser Gly Ser Ala Ser Gly Ser Gly Ser
 20 25 30
 Gly Ser Ser Ser Gly Ser Ser Asp Gly Ser Ser Ser Gln Ser Gly
 35 40 45
 Ser Ser Asp Ser Asp Ser Gly Ser Glu Ser Gly Ser Gln Ser Glu Ser
 50 55 60
 Glu Ser Asp Thr Ser Arg Glu Asn Lys Val Gln Ala Lys Pro Pro Lys
 65 70 75 80
 Val Asp Gly Ala Glu Phe Trp Lys Ser Ser Pro Ser Ile Leu Ala Val
 85 90 95
 Gln Arg Ser Ala Ile Leu Lys Lys Gln Gln Gln Gln Gln Gln Gln
 100 105 110
 Gln His Gln Ala Ser Ser Asn Ser Gly Ser Glu Glu Asp Ser Ser Ser
 115 120 125
 Ser Glu Asp Ser Asp Asp Ser Ser Ser Glu Val Lys Arg Lys Lys His
 130 135 140
 Lys Asp Glu Asp Trp Gln Met Ser Gly Ser Gly Ser Pro Ser Gln Ser
 145 150 155 160
 Gly Ser Asp Ser Glu Ser Glu Glu Arg Glu Lys Ser Ser Cys Asp
 165 170 175
 Glu Thr Glu Ser Asp Tyr Glu Pro Lys Asn Lys Val Lys Ser Arg Lys
 180 185 190
 Pro Gln Asn Arg Ser Lys Ser Lys Asn Gly Lys Lys Ile Leu Gly Gln
 195 200 205
 Lys Lys Arg Gln Ile Asp Ser Ser Glu Glu Asp Asp Asp Glu Glu Asp
 210 215 220
 Tyr Asp Asn Asp Lys Arg Ser Ser Arg Arg Gln Ala Thr Val Asn Val
 225 230 235 240
 Ser Tyr Lys Glu Asp Glu Met Lys Thr Asp Ser Asp Asp Leu Leu
 245 250 255
 Glu Val Cys Gly Glu Asp Val Pro Gln Pro Glu Glu Glu Phe Glu
 260 265 270
 Thr Ile Glu Arg Phe Met Asp Cys Arg Ile Gly Arg Lys Gly Ala Thr
 275 280 285

311

Gly Ala Thr Thr Ile Tyr Ala Val Glu Ala Asp Gly Asp Pro Asn
290 295 300
Ala Gly Phe Glu Lys Asn Lys Glu Pro Gly Glu Ile Gln Tyr Leu Ile
305 310 315 320
Lys Trp Lys Gly Trp Ser His Ile His Asn Thr Trp Glu Thr Glu Glu
325 330 335
Thr Leu Lys Gln Gln Asn Val Arg Gly Met Lys Lys Leu Asp Asn Tyr
340 345 350
Lys Lys Lys Asp Gln Glu Thr Lys Arg Trp Leu Lys Asn Ala Ser Pro
355 360 365
Glu Asp Val Glu Tyr Tyr Asn Cys Gln Gln Glu Leu Thr Asp Asp Leu
370 375 380
His Lys Gln Tyr Gln Ile Val Gly Arg Ile Ile Ala His Ser Asn Gln
385 390 395 400
Lys Ser Ala Ala Gly Tyr Pro Asp Tyr Tyr Cys Lys Trp Gln Gly Leu
405 410 415
Pro Tyr Ser Glu Cys Ser Trp Glu Asp Gly Ala Leu Ile Ser Lys Lys
420 425 430
Phe Gln Ala Cys Ile Asp Glu Tyr Phe Ser Arg Asn Gln Ser Lys Thr
435 440 445
Thr Pro Phe Lys Asp Cys Lys Val Leu Lys Gln Arg Pro Arg Phe Val
450 455 460
Ala Leu Lys Lys Gln Pro Ser Tyr Ile Gly Gly His Glu Gly Leu Glu
465 470 475 480
Leu Arg Asp Tyr Gln Leu Asn Gly Leu Asn Trp Leu Ala His Ser Trp
485 490 495
Cys Lys Gly Asn Ser Cys Ile Leu Ala Asp Glu Met Gly Leu Gly Lys
500 505 510
Thr Ile Gln Thr Ile Ser Phe Leu Asn Tyr Leu Phe His Glu His Gln
515 520 525
Leu Tyr Gly Pro Phe Leu Leu Val Val Pro Leu Ser Thr Leu Thr Ser
530 535 540
Trp Gln Arg Glu Ile Gln Thr Trp Ala Ser Gln Met Asn Ala Val Val
545 550 555 560
Tyr Leu Gly Asp Ile Asn Ser Arg Asn Met Ile Arg Thr His Glu Trp
565 570 575
Thr His His Gln Thr Lys Arg Leu Lys Phe Asn Ile Leu Leu Thr Thr
580 585 590
Tyr Glu Ile Leu Leu Lys Asp Lys Ala Phe Leu Gly Gly Leu Asn Trp
595 600 605
Ala Phe Ile Gly Val Asp Glu Ala His Arg Leu Lys Asn Asp Ser
610 615 620

312

Leu Leu Tyr Lys Thr Leu Ile Asp Phe Lys Ser Asn His Arg Leu Leu
625 630 635 640
Ile Thr Gly Thr Pro Leu Gln Asn Ser Leu Lys Glu Leu Trp Ser Leu
645 650 655
Leu His Phe Ile Met Pro Glu Lys Phe Ser Ser Trp Glu Asp Phe Glu
660 665 670
Glu Glu His Gly Lys Gly Arg Glu Tyr Gly Tyr Ala Ser Leu His Lys
675 680 685
Glu Leu Glu Pro Phe Leu Leu Arg Arg Val Lys Lys Asp Val Glu Lys
690 695 700
Ser Leu Pro Ala Lys Val Glu Gln Ile Leu Arg Met Glu Met Ser Ala
705 710 715 720
Leu Gln Lys Gln Tyr Tyr Lys Trp Ile Leu Thr Arg Asn Tyr Lys Ala
725 730 735
Leu Ser Lys Gly Ser Lys Gly Ser Thr Ser Gly Phe Leu Asn Ile Met
740 745 750
Met Glu Leu Lys Lys Cys Cys Asn His Cys Tyr Leu Ile Lys Pro Pro
755 760 765
Asp Asn Asn Glu Phe Tyr Asn Lys Gln Glu Ala Leu Gln His Leu Ile
770 775 780
Arg Ser Ser Gly Lys Leu Ile Leu Leu Asp Lys Leu Leu Ile Arg Leu
785 790 795 800
Arg Glu Arg Gly Asn Arg Val Leu Ile Phe Ser Gln Met Val Arg Met
805 810 815
Leu Asp Ile Leu Ala Glu Tyr Leu Lys Tyr Arg Gln Phe Pro Phe Gln
820 825 830
Arg Leu Asp Gly Ser Ile Lys Gly Glu Leu Arg Lys Gln Ala Leu Asp
835 840 845
His Phe Asn Ala Glu Gly Ser Glu Asp Phe Cys Phe Leu Leu Ser Thr
850 855 860
Arg Ala Gly Gly Leu Gly Ile Asn Leu Ala Ser Ala Asp Thr Val Val
865 870 875 880
Ile Phe Asp Ser Asp Trp Asn Pro Gln Asn Asp Leu Gln Ala Gln Ala
885 890 895
Arg Ala His Arg Ile Gly Gln Lys Lys Gln Val Asn Ile Tyr Arg Leu
900 905 910
Val Thr Lys Gly Ser Val Glu Glu Asp Ile Leu Glu Arg Ala Lys Lys
915 920 925
Lys Met Val Leu Asp His Leu Val Ile Gln Arg Met Asp Thr Thr Gly
930 935 940
Lys Thr Val Leu His Thr Gly Ser Ala Pro Ser Ser Ser Thr Pro Phe

313

945	950	955	960
Asn Lys Glu Glu Leu Ser Ala Ile Leu Lys Phe Gly Ala Glu Glu Leu	965	970	975
Phe Lys Glu Pro Glu Gly Glu Glu Glu Glu Glu Glu Pro Glu Glu Met Asp Ile	980	985	990
Asp Glu Ile Leu Lys Arg Ala Glu Thr His Glu Asn Glu Pro Gly Pro	995	1000	1005
Leu Thr Val Gly Asp Glu Leu Leu Ser Gln Phe Lys Val Ala Asn	1010	1015	1020
Phe Ser Asn Met Asp Glu Asp Ile Glu Leu Glu Pro Glu Arg	1025	1030	1035
Asn Ser Lys Asn Trp Glu Glu Ile Ile Pro Glu Asp Gln Arg Arg	1040	1045	1050
Arg Leu Glu Glu Glu Arg Gln Lys Glu Leu Glu Glu Ile Tyr	1055	1060	1065
Met Leu Pro Arg Met Arg Asn Cys Ala Lys Gln Ile Ser Phe Asn	1070	1075	1080
Gly Ser Glu Gly Arg Arg Ser Arg Ser Arg Arg Tyr Ser Gly Ser	1085	1090	1095
Asp Ser Asp Ser Ile Ser Glu Gly Lys Arg Pro Lys Lys Arg Gly	1100	1105	1110
Arg Pro Arg Thr Ile Pro Arg Glu Asn Ile Lys Gly Phe Ser Asp	1115	1120	1125
Ala Glu Ile Arg Arg Phe Ile Lys Ser Tyr Lys Lys Phe Gly Gly	1130	1135	1140
Pro Leu Glu Arg Leu Asp Ala Ile Ala Arg Asp Ala Glu Leu Val	1145	1150	1155
Asp Lys Ser Glu Thr Asp Leu Arg Arg Leu Gly Glu Leu Val His	1160	1165	1170
Asn Gly Cys Ile Lys Ala Leu Lys Asp Ser Ser Ser Gly Thr Glu	1175	1180	1185
Arg Thr Gly Gly Arg Leu Gly Lys Val Lys Gly Pro Thr Phe Arg	1190	1195	1200
Ile Ser Gly Val Gln Val Asn Ala Lys Leu Val Ile Ser His Glu	1205	1210	1215
Glu Glu Leu Ile Pro Leu His Lys Ser Ile Pro Ser Asp Pro Glu	1220	1225	1230
Glu Arg Lys Gln Tyr Thr Ile Pro Cys His Thr Lys Ala Ala His	1235	1240	1245
Phe Asp Ile Asp Trp Gly Lys Glu Asp Asp Ser Asn Leu Leu Ile	1250	1255	1260

Gly Ile	Tyr Glu Tyr Gly Tyr	Gly Ser Trp Glu Met	Ile Lys Met
1265		1270	1275
Asp Pro	Asp Leu Ser Leu Thr	His Lys Ile Leu Pro	Asp Asp Pro
1280		1285	1290
Asp Lys	Lys Pro Gln Ala Lys	Gln Leu Gln Thr Arg	Ala Asp Tyr
1295		1300	1305
Leu Ile	Lys Leu Leu Ser Arg	Asp Leu Ala Lys Lys	Glu Ala Leu
1310		1315	1320
Ser Gly	Ala Gly Ser Ser Lys	Arg Arg Lys Ala Arg	Ala Lys Lys
1325		1330	1335
Asn Lys	Ala Met Lys Ser Ile	Lys Val Lys Glu Glu	Ile Lys Ser
1340		1345	1350
Asp Ser	Ser Pro Leu Pro Ser	Glu Lys Ser Asp Glu	Asp Asp Asp
1355		1360	1365
Lys Leu	Ser Glu Ser Lys Ser	Asp Gly Arg Glu Arg	Ser Lys Lys
1370		1375	1380
Ser Ser	Val Ser Asp Ala Pro	Val His Ile Thr Ala	Ser Gly Glu
1385		1390	1395
Pro Val	Pro Ile Ser Glu Glu	Ser Glu Glu Leu Asp	Gln Lys Thr
1400		1405	1410
Phe Ser	Ile Cys Lys Glu Arg	Met Arg Pro Val Lys	Ala Ala Leu
1415		1420	1425
Lys Gln	Leu Asp Arg Pro Glu	Lys Gly Leu Ser Glu	Arg Glu Gln
1430		1435	1440
Leu Glu	His Thr Arg Gln Cys	Leu Ile Lys Ile Gly	Asp His Ile
1445		1450	1455
Thr Glu	Cys Leu Lys Glu Tyr	Thr Asn Pro Glu Gln	Ile Lys Gln
1460		1465	1470
Trp Arg	Lys Asn Leu Trp Ile	Phe Val Ser Lys Phe	Thr Glu Phe
1475		1480	1485
Asp Ala	Arg Lys Leu His Lys	Leu Tyr Lys His Ala	Ile Lys Lys
1490		1495	1500
Arg Gln	Glu Ser Gln Gln Asn	Ser Asp Gln Asn Ser	Asn Leu Asn
1505		1510	1515
Pro His	Val Ile Arg Asn Pro	Asp Val Glu Arg Leu	Lys Glu Asn
1520		1525	1530
Thr Asn	His Asp Asp Ser Ser	Arg Asp Ser Tyr Ser	Ser Asp Arg
1535		1540	1545
His Leu	Thr Gln Tyr His Asp	His His Lys Asp Arg	His Gln Gly
1550		1555	1560
Asp Ser	Tyr Lys Lys Ser Asn	Ser Arg Lys Arg Pro	Tyr Ser Ser
1565		1570	1575

Phe Ser Asn Gly Lys Asp His Arg Asp Trp Asp His Tyr Lys Gln
 1580 1585 1590
 Asp Ser Arg Tyr Tyr Ser Asp Arg Glu Lys His Arg Lys Leu Asp
 1595 1600 1605
 Asp His Arg Ser Arg Asp His Arg Ser Asn Leu Glu Gly Ser Leu
 1610 1615 1620
 Lys Asp Arg Ser His Ser Asp His Arg Ser His Ser Asp His Arg
 1625 1630 1635
 Leu His Ser Asp His Arg Ser Ser Ser Glu Tyr Thr His His Lys
 1640 1645 1650
 Ser Ser Arg Asp Tyr Arg Tyr His Ser Asp Trp Gln Met Asp His
 1655 1660 1665
 Arg Ala Ser Ser Ser Gly Pro Arg Ser Pro Leu Asp Gln Arg Ser
 1670 1675 1680
 Tyr Gly Ser Arg Ser Pro Phe Glu His Ser Val Glu His Lys Ser
 1685 1690 1695
 Thr Pro Glu His Thr Trp Ser Ser Arg Lys Thr
 1700 1705
 <210> 160
 <211> 437
 <212> PRT
 <213> Homo sapiens
 <400> 160
 Ser Cys Ser Pro His Ala Thr Leu Gly Pro Gln Pro Cys Arg Val Leu
 1 5 10 15
 Phe Ser Met Ser Phe Ile Pro Val Ala Glu Asp Ser Asp Phe Pro Ile
 20 25 30
 His Asn Leu Pro Tyr Gly Val Phe Ser Thr Arg Gly Asp Pro Arg Pro
 35 40 45
 Arg Ile Gly Val Ala Ile Gly Asp Gln Ile Leu Asp Leu Ser Ile Ile
 50 55 60
 Lys His Leu Phe Thr Gly Pro Val Leu Ser Lys His Gln Asp Val Phe
 65 70 75 80
 Asn Gln Pro Thr Leu Asn Ser Phe Met Gly Leu Gly Gln Ala Ala Trp
 85 90 95
 Lys Glu Ala Arg Val Phe Leu Gln Asn Leu Leu Ser Val Ser Gln Ala
 100 105 110
 Arg Leu Arg Asp Asp Thr Glu Leu Arg Lys Cys Ala Phe Ile Ser Gln
 115 120 125
 Ala Ser Ala Thr Met His Leu Pro Ala Thr Ile Gly Asp Tyr Thr Asp
 130 135 140
 Phe Tyr Ser Ser Arg Gln His Ala Thr Asn Val Gly Ile Met Phe Arg

145 150 155 160
 Asp Lys Glu Asn Ala Leu Met Pro Asn Trp Leu His Leu Pro Val Gly
 165 170 175
 Tyr His Gly Arg Ala Ser Ser Val Val Val Ser Gly Thr Pro Ile Arg
 180 185 190
 Arg Pro Met Gly Gln Met Lys Pro Asp Asp Ser Lys Pro Pro Val Tyr
 195 200 205
 Gly Ala Cys Lys Leu Leu Asp Met Glu Leu Met Ala Phe Phe Val
 210 215 220
 Gly Pro Gly Asn Arg Leu Gly Glu Pro Ile Pro Ile Ser Lys Ala His
 225 230 235 240
 Glu His Ile Phe Gly Met Val Leu Met Asn Asp Trp Ser Ala Arg Asp
 245 250 255
 Ile Gln Lys Trp Glu Tyr Val Pro Leu Gly Pro Phe Leu Gly Lys Ser
 260 265 270
 Phe Gly Thr Thr Val Ser Pro Trp Val Val Pro Met Asp Ala Leu Met
 275 280 285
 Pro Phe Ala Val Pro Asn Pro Lys Gln Asp Pro Arg Pro Leu Pro Tyr
 290 295 300
 Leu Cys His Asp Glu Pro Tyr Thr Phe Asp Ile Asn Leu Ser Val Asn
 305 310 315 320
 Leu Lys Gly Glu Gly Met Ser Gln Ala Ala Thr Ile Cys Lys Ser Asn
 325 330 335
 Phe Lys Tyr Met Tyr Trp Thr Met Leu Gln Gln Leu Thr His His Ser
 340 345 350
 Val Asn Gly Cys Asn Leu Arg Pro Gly Asp Leu Leu Ala Ser Gly Thr
 355 360 365
 Ile Ser Gly Pro Glu Pro Glu Asn Phe Gly Ser Met Leu Glu Leu Ser
 370 375 380
 Trp Lys Gly Thr Lys Pro Ile Asp Leu Gly Asn Gly Gln Thr Arg Lys
 385 390 395 400
 Phe Leu Leu Asp Gly Asp Glu Val Ile Ile Thr Gly Tyr Cys Gln Gly
 405 410 415
 Asp Gly Tyr Arg Ile Gly Phe Gly Gln Cys Ala Gly Lys Val Leu Pro
 420 425 430
 Ala Leu Leu Pro Ser
 435
 <210> 161
 <211> 580
 <212> PRT
 <213> Homo sapiens
 <400> 161

Met Lys Asp Arg Leu Tyr Phe Ala Thr Leu Arg Asn Arg Pro Lys Ser
1 5 10 15
Thr Val Asn Thr His Tyr Phe Ser Ile Asp Glu Glu Leu Val Tyr Glu
20 25 30
Asn Phe Tyr Ala Asp Phe Gly Pro Leu Asn Leu Ala Met Val Tyr Arg
35 40 45
Tyr Cys Cys Lys Leu Asn Lys Lys Leu Lys Ser Tyr Ser Leu Ser Arg
50 55 60
Lys Lys Ile Val His Tyr Thr Cys Phe Asp Gln Arg Lys Arg Ala Asn
65 70 75 80
Ala Ala Phe Leu Ile Gly Ala Tyr Ala Val Ile Tyr Leu Lys Lys Thr
85 90 95
Pro Glu Glu Ala Tyr Arg Ala Leu Leu Ser Gly Ser Asn Pro Tyr
100 105 110
Leu Pro Phe Arg Asp Ala Ser Phe Gly Asn Cys Thr Tyr Asn Leu Thr
115 120 125
Ile Leu Asp Cys Leu Gln Gly Ile Arg Lys Gly Leu Gln His Gly Phe
130 135 140
Phe Asp Phe Glu Thr Ile Asp Val Asp Glu Tyr Glu His Tyr Glu Arg
145 150 155 160
Val Glu Asn Gly Asp Phe Asn Cys Ile Val Pro Gly Lys Phe Leu Ala
165 170 175
Phe Ser Gly Pro His Pro Lys Ser Lys Ile Glu Asn Gly Tyr Pro Leu
180 185 190
His Ala Pro Glu Ala Tyr Phe Pro Tyr Phe Lys Lys His Asn Val Thr
195 200 205
Ala Val Val Arg Leu Asn Lys Lys Ile Tyr Glu Ala Lys Arg Phe Thr
210 215 220
Asp Ala Gly Phe Glu His Tyr Asp Leu Phe Phe Ile Asp Gly Ser Thr
225 230 235 240
Pro Ser Asp Asn Ile Val Arg Arg Phe Leu Asn Ile Cys Glu Asn Thr
245 250 255
Glu Gly Ala Ile Ala Val His Cys Lys Ala Gly Leu Gly Arg Thr Gly
260 265 270
Thr Leu Ile Ala Cys Tyr Val Met Lys His Tyr Arg Phe Thr His Ala
275 280 285
Glu Ile Ile Ala Trp Ile Arg Ile Cys Arg Pro Gly Ser Ile Ile Gly
290 295 300
Pro Gln Gln His Phe Leu Glu Glu Lys Gln Ala Ser Leu Trp Val Gln
305 310 315 320
Gly Asp Ile Phe Arg Ser Lys Leu Lys Asn Arg Pro Ser Ser Glu Gly
325 330 335

318

Ser Ile Asn Lys Ile Leu Ser Gly Leu Asp Asp Met Ser Ile Gly Gly
340 345 350
Asn Leu Ser Lys Thr Gln Asn Met Glu Arg Phe Gly Glu Asp Asn Leu
355 360 365
Glu Asp Asp Val Glu Met Lys Asn Gly Ile Thr Gln Gly Asp Lys
370 375 380
Leu Arg Ala Leu Lys Ser Gln Arg Gln Pro Arg Thr Ser Pro Ser Cys
385 390 395 400
Ala Phe Arg Ser Asp Asp Thr Lys Gly His Pro Arg Ala Val Ser Gln
405 410 415
Pro Phe Arg Leu Ser Ser Ser Leu Gln Gly Ser Ala Val Thr Leu Lys
420 425 430
Thr Ser Lys Met Ala Leu Ser Pro Ser Ala Thr Ala Lys Arg Ile Asn.
435 440 445
Arg Thr Ser Leu Ser Ser Gly Ala Thr Val Arg Ser Phe Ser Ile Asn
450 455 460
Ser Arg Leu Ala Ser Ser Leu Gly Asn Leu Asn Ala Ala Thr Asp Asp
465 470 475 480
Pro Glu Asn Lys Lys Thr Ser Ser Ser Lys Ala Gly Phe Thr Ala
485 490 495
Ser Pro Phe Thr Asn Leu Leu Asn Gly Ser Ser Gln Pro Thr Thr Arg
500 505 510
Asn Tyr Pro Glu Leu Asn Asn Asn Gln Tyr Asn Arg Ser Ser Asn Ser
515 520 525
Asn Gly Gly Asn Leu Asn Ser Pro Pro Gly Pro His Ser Ala Lys Thr
530 535 540
Glu Glu His Thr Thr Ile Leu Arg Pro Ser Tyr Thr Gly Leu Ser Ser
545 550 555 560
Ser Ser Ala Arg Phe Leu Ser Arg Ser Ile Pro Ser Leu Gln Ser Glu
565 570 575
Tyr Val His Tyr
580
<210> 162
<211> 447
<212> PRT
<213> Homo sapiens
<400> 162
Met Arg Ser Ser Thr Leu Gln Asp Pro Arg Arg Arg Asp Pro Gln Asp
1 5 10 15
Asp Val Tyr Val Asp Ile Thr Asp Arg Leu Arg Phe Ala Ile Leu Tyr
20 25 30
Ser Arg Pro Lys Ser Ala Ser Asn Val His Tyr Phe Ser Ile Asp Asn

319

35 40 45
 Glu Leu Glu Tyr Glu Asn Phe Ser Glu Asp Phe Gly Pro Leu Asn Leu 60
 50
 Ala Met Val Tyr Arg Tyr Cys Cys Lys Ile Asn Lys Lys Leu Lys Ser 80
 65 70 75
 Ile Thr Met Leu Arg Lys Lys Ile Val His Phe Thr Gly Ser Asp Gln 95
 85 90
 Arg Lys Gln Ala Asn Ala Ala Phe Leu Val Gly Cys Tyr Met Val Ile 110
 100 105
 Tyr Leu Gly Arg Thr Pro Glu Ala Ala Tyr Arg Ile Leu Ile Phe Gly 125
 115 120
 Asp Thr Pro Tyr Ile Pro Phe Arg Asp Ala Ala Tyr Gly Ser Cys Asn 140
 130 135
 Phe Tyr Ile Thr Leu Leu Asp Cys Phe His Ala Val Lys Lys Ala Met 160
 145 150 155
 Gln Tyr Gly Phe Leu Asn Phe Asn Ser Phe Asn Leu Asp Glu Tyr Glu 175
 165 170
 His Tyr Glu Lys Ala Glu Asn Gly Asp Leu Asn Trp Ile Ile Pro Asp 190
 180 185
 Arg Phe Ile Ala Phe Cys Gly Pro His Ser Arg Ala Arg Leu Glu Ser 205
 195 200
 Gly Tyr His Gln His Ser Pro Glu Thr Tyr Ile Gln Tyr Phe Lys Asn 220
 210 215
 His Asn Val Thr Thr Ile Ile Arg Leu Asn Lys Arg Met Tyr Asp Ala 240
 225 230 235
 Lys Arg Phe Thr Asp Ala Gly Phe Asp His His Asp Leu Phe Ala 255
 245 250
 Asp Gly Ser Thr Pro Thr Asp Ala Ile Val Lys Arg Phe Leu Asp Ile 270
 260 265
 Cys Glu Asn Ala Glu Gly Ala Ile Ala Val His Cys Lys Lys Ala Gly Leu 285
 275 280
 Gly Arg Thr Gly Thr Leu Ile Ala Cys Tyr Ile Met Lys His Tyr Arg 300
 290 295
 Met Thr Ala Ala Glu Thr Ile Ala Trp Val Arg Ile Cys Arg Pro Gly 320
 305 310 315
 Leu Val Ile Gly Pro Gln Gln Phe Leu Val Met Lys Gln Thr Ser 335
 325 330
 Leu Trp Leu Glu Gly Asp Tyr Phe Arg Gln Arg Leu Lys Gly Gln Glu 350
 340 345
 Asn Gly Gln His Arg Ala Ala Phe Ser Lys Leu Leu Ser Gly Val Asp 365
 355 360

320

Asp Ile Ser Ile Asn Gly Val Glu Asn Gln Asp Gln Gln Glu Pro Lys 370
 375 380
 Pro Tyr Ser Asp Asp Asp Glu Ile Asn Gly Val Thr Gln Gly Asp Arg 400
 385 390 395
 Ser Arg Ala Leu Lys Arg Arg Arg Gln Ser Lys Thr Asn Asp Ile Leu 415
 405 410
 Leu Pro Ser Pro Leu Ala Val Leu Thr Phe Thr Leu Cys Ser Val Val 430
 420 425
 Ile Trp Trp Ile Val Cys Asp Tyr Ile Leu Pro Ile Leu Leu Phe 445
 435 440
 <210> 163
 <211> 159
 <212> PRT
 <213> Homo sapiens
 <400> 163
 Met Ala Val Leu Trp Arg Leu Ser Ala Val Cys Gly Ala Leu Gly Gly 15
 1 10
 Arg Ala Leu Leu Arg Thr Pro Val Val Arg Pro Ala His Ile Ser 30
 20 25
 Ala Phe Leu Gln Asp Arg Pro Ile Pro Glu Trp Cys Gly Val Gln His 45
 35 40
 Ile His Leu Ser Pro Ser His His Ser Gly Ser Lys Ala Ala Ser Leu 60
 50 55
 His Trp Thr Ser Glu Arg Val Val Ser Val Leu Leu Leu Gly Leu Leu 80
 65 70 75
 Pro Ala Ala Tyr Leu Asn Pro Cys Ser Ala Met Asp Tyr Ser Leu Ala 95
 85 90
 Ala Ala Leu Thr Leu His Gly His Trp Gly Leu Gly Gln Val Val Thr 110
 100 105
 Asp Tyr Val His Gly Asp Ala Leu Gln Lys Ala Ala Lys Ala Gly Leu 135
 115 120
 Leu Ala Leu Ser Ala Leu Thr Phe Ala Gly Leu Cys Tyr Phe Asn Tyr 140
 130 135
 His Asp Val Gly Ile Cys Lys Lys Ala Val Ala Met Leu Trp Lys Leu 155
 145 150
 <210> 164
 <211> 1924
 <212> PRT
 <213> Homo sapiens
 <400> 164
 Met Lys Ser Pro Ala Leu Gln Pro Leu Ser Met Ala Gly Leu Gln Leu 15
 1 5 10
 Met Thr Pro Ala Ser Ser Pro Met Gly Pro Phe Phe Gly Leu Pro Trp 30
 20 25

321

Gln Gln Glu Ala Ile His Asp Asn Ile Tyr Thr Pro Arg Lys Tyr Gln
35 40 45
Val Glu Leu Leu Glu Ala Ala Leu Asp His Asn Thr Ile Val Cys Leu
50 55 60
Asn Thr Gly Ser Gly Lys Thr Phe Ile Ala Ser Thr Thr Thr Leu Lys
65 70 75 80
Ser Cys Leu Tyr Leu Asp Leu Gly Glu Thr Ser Ala Arg Asn Gly Lys
85 90 95
Arg Thr Val Phe Leu Val Asn Ser Ala Asn Gln Val Ala Gln Gln Val
100 105 110
Ser Ala Val Arg Thr His Ser Asp Leu Lys Val Gly Glu Tyr Ser Asn
115 120 125
Leu Glu Val Asn Ala Ser Trp Thr Lys Glu Arg Trp Asn Gln Glu Phe
130 135 140
Thr Lys His Gln Val Leu Ile Met Thr Cys Tyr Val Ala Leu Asn Val
145 150 155 160
Leu Lys Asn Gly Tyr Leu Ser Leu Ser Asp Ile Asn Leu Leu Val Phe
165 170 175
Asp Glu Cys His Leu Ala Ile Leu Asp His Pro Tyr Arg Glu Phe Met
180 185 190
Lys Leu Cys Glu Ile Cys Pro Ser Cys Pro Arg Ile Leu Gly Leu Thr
195 200 205
Ala Ser Ile Leu Asn Gly Lys Trp Asp Pro Glu Asp Leu Glu Lys
210 215 220
Phe Gln Lys Leu Glu Lys Ile Leu Lys Ser Asn Ala Glu Thr Ala Thr
225 230 235 240
Asp Leu Val Val Leu Asp Arg Tyr Thr Ser Gln Pro Cys Glu Ile Val
245 250 255
Val Asp Cys Gly Pro Phe Thr Asp Arg Ser Gly Leu Tyr Glu Arg Leu
260 265 270
Leu Met Glu Leu Glu Glu Ala Leu Asn Phe Ile Asn Asp Cys Asn Ile
275 280 285
Ser Val His Ser Lys Glu Arg Asp Ser Thr Leu Ile Ser Lys Gln Ile
290 295 300
Leu Ser Asp Cys Arg Ala Val Leu Val Val Leu Gly Pro Trp Cys Ala
305 310 315 320
Asp Lys Val Ala Gly Met Met Val Arg Glu Leu Gln Lys Tyr Ile Lys
325 330 335
His Glu Gln Glu Glu Leu His Arg Lys Phe Leu Leu Phe Thr Asp Thr
340 345 350
Phe Leu Arg Lys Ile His Ala Leu Cys Glu Glu His Phe Ser Pro Ala

322

Ser Leu Asp Leu Lys Phe Val Thr Pro Lys Val Ile Lys Leu Leu Glu
355 360 365
370 375 380
Ile Leu Arg Lys Tyr Lys Pro Tyr Glu Arg His Ser Phe Glu Ser Val
385 390 395 400
Glu Trp Tyr Asn Asn Arg Asn Gln Asp Asn Tyr Val Ser Trp Ser Asp
405 410 415
Ser Glu Asp Asp Asp Glu Asp Glu Glu Ile Glu Glu Lys Glu Lys Pro
420 425 430
Glu Thr Asn Phe Pro Ser Pro Phe Thr Asn Ile Leu Cys Gly Ile Ile
435 440 445
Phe Val Glu Arg Arg Tyr Thr Ala Val Val Leu Asn Arg Leu Ile Lys
450 455 460
Glu Ala Gly Lys Gln Asp Pro Glu Leu Ala Tyr Ile Ser Ser Asn Phe
465 470 475 480
Ile Thr Gly His Gly Ile Gly Lys Asn Gln Pro Arg Asn Asn Thr Met
485 490 495
Glu Ala Glu Phe Arg Lys Gln Glu Val Leu Arg Lys Phe Arg Ala
500 505 510
His Glu Thr Asn Leu Leu Ile Ala Thr Ser Ile Val Glu Glu Gly Val
515 520 525
Asp Ile Pro Lys Cys Asn Leu Val Val Arg Phe Asp Leu Pro Thr Glu
530 535 540
Tyr Arg Ser Tyr Val Gln Ser Lys Gly Arg Ala Arg Ala Pro Ile Ser
545 550 555 560
Asn Tyr Ile Met Leu Ala Asp Thr Asp Lys Ile Lys Ser Phe Glu Glu
565 570 575
Asp Leu Lys Thr Tyr Lys Ala Ile Glu Lys Ile Leu Arg Asn Lys Cys
580 585 590
Ser Lys Ser Val Asp Thr Gly Glu Thr Asp Ile Asp Pro Val Met Asp
595 600 605
Asp Asp His Val Phe Pro Pro Tyr Val Leu Arg Pro Asp Asp Gly Gly
610 615 620
Pro Arg Val Thr Ile Asn Thr Ala Ile Gly His Ile Asn Arg Tyr Cys
625 630 635 640
Ala Arg Leu Pro Ser Asp Pro Phe Thr His Leu Ala Pro Lys Cys Arg
645 650 655
Thr Arg Glu Leu Pro Asp Gly Thr Phe Tyr Ser Thr Thr Leu Pro
660 665 670
Ile Asn Ser Pro Leu Arg Ala Ser Ile Val Gly Pro Pro Met Ser Cys
675 680 685

323

Val Arg Leu Ala Glu Arg Val Val Ala Leu Ile Cys Cys Glu Lys Leu 690 700
 His Lys Ile Gly Glu Leu Asp Asp His Leu Met Pro Val Gly Lys Glu 705 710 715 720
 Thr Val Lys Tyr Glu Glu Glu Leu Asp Leu His Asp Glu Glu Thr 725 730 735
 Ser Val Pro Gly Arg Pro Gly Ser Thr Lys Arg Arg Glu Cys Tyr Pro 740 745 750
 Lys Ala Ile Pro Glu Cys Leu Arg Asp Ser Tyr Pro Arg Pro Asp Glu 755 760 765
 Pro Cys Tyr Leu Tyr Val Ile Gly Met Val Leu Thr Thr Pro Leu Pro 770 775 780
 Asp Glu Leu Asn Phe Arg Arg Arg Lys Leu Tyr Pro Pro Glu Asp Thr 785 790 795 800
 Thr Arg Cys Phe Gly Ile Leu Thr Ala Lys Pro Ile Pro Glu Ile Pro 805 810 815
 His Phe Pro Val Tyr Thr Arg Ser Gly Glu Val Thr Ile Ser Ile Glu 820 825 830
 Leu Lys Lys Ser Gly Phe Met Leu Ser Leu Glu Met Leu Glu Ile 835 840 845
 Thr Arg Leu His Glu Tyr Ile Phe Ser His Ile Leu Arg Leu Glu Lys 850 855 860
 Pro Ala Leu Glu Phe Lys Pro Thr Asp Ala Asp Ser Ala Tyr Cys Val 865 870 875 880
 Leu Pro Leu Asn Val Val Asn Asp Ser Thr Leu Asp Ile Asp Phe 885 890 895
 Lys Phe Met Glu Asp Ile Glu Lys Ser Glu Ala Arg Ile Gly Ile Pro 900 905 910
 Ser Thr Lys Tyr Thr Lys Glu Thr Pro Phe Val Phe Lys Leu Glu Asp 915 920 925
 Tyr Glu Asp Ala Val Ile Ile Pro Arg Tyr Arg Asn Phe Asp Glu Pro 930 935 940
 His Arg Phe Tyr Val Ala Asp Val Tyr Thr Asp Leu Thr Pro Leu Ser 945 950 955 960
 Lys Phe Pro Ser Pro Glu Tyr Glu Thr Phe Ala Glu Tyr Tyr Lys Thr 965 970 975
 Lys Tyr Asn Leu Asp Leu Thr Asn Leu Asn Glu Pro Leu Leu Asp Val 980 985 990
 Asp His Thr Ser Ser Arg Leu Asn Leu Leu Thr Pro Arg His Leu Asn 995 1000 1005
 Glu Lys Gly Lys Ala Leu Pro Leu Ser Ser Ala Glu Lys Arg Lys 1010 1015 1020

Ala Lys Trp Glu Ser Leu Gln Asn Lys Gln Ile Leu Val Pro Glu 1025 1030 1035
 Leu Cys Ala Ile His Pro Ile Pro Ala Ser Leu Trp Arg Lys Ala 1040 1045 1050
 Val Cys Leu Pro Ser Ile Leu Tyr Arg Leu His Cys Leu Leu Thr 1055 1060 1065
 Ala Glu Glu Leu Arg Ala Gln Thr Ala Ser Asp Ala Gly Val Gly 1070 1075 1080
 Val Arg Ser Leu Pro Ala Asp Phe Arg Tyr Pro Asn Leu Asp Phe 1085 1090 1095
 Gly Trp Lys Lys Ser Ile Asp Ser Lys Ser Phe Ile Ser Ile Ser 1100 1105 1110
 Asn Ser Ser Ser Ala Glu Asn Asp Asn Tyr Cys Lys His Ser Thr 1115 1120 1125
 Ile Val Pro Glu Asn Ala Ala His Gln Gly Ala Asn Arg Thr Ser 1130 1135 1140
 Ser Leu Glu Asn His Asp Gln Met Ser Val Asn Cys Arg Thr Leu 1145 1150 1155
 Leu Ser Glu Ser Pro Gly Lys Leu His Val Glu Val Ser Ala Asp 1160 1165 1170
 Leu Thr Ala Ile Asn Gly Leu Ser Tyr Asn Gln Asn Leu Ala Asn 1175 1180 1185
 Gly Ser Tyr Asp Leu Ala Asn Arg Asp Phe Cys Gln Gly Asn Gln 1190 1195 1200
 Leu Asn Tyr Tyr Lys Gln Glu Ile Pro Val Gln Pro Thr Thr Ser 1205 1210 1215
 Tyr Ser Ile Gln Asn Leu Tyr Ser Tyr Glu Asn Gln Pro Gln Pro 1220 1225 1230
 Ser Asp Glu Cys Thr Leu Leu Ser Asn Lys Tyr Leu Asp Gly Asn 1235 1240 1245
 Ala Asn Lys Ser Thr Ser Asp Gly Ser Pro Val Met Ala Val Met 1250 1255 1260
 Pro Gly Thr Thr Asp Thr Ile Gln Val Leu Lys Gly Arg Met Asp 1265 1270 1275
 Ser Glu Gln Ser Pro Ser Ile Gly Tyr Ser Ser Arg Thr Leu Gly 1280 1285 1290
 Pro Asn Pro Gly Leu Ile Leu Gln Ala Leu Thr Leu Ser Asn Ala 1295 1300 1305
 Ser Asp Gly Phe Asn Leu Glu Arg Leu Glu Met Leu Gly Asp Ser 1310 1315 1320
 Phe Leu Lys His Ala Ile Thr Thr Tyr Leu Phe Cys Thr Tyr Pro 1325

1335 1330 1335
 Asp Ala His Glu Gly Arg Leu Ser Tyr Met Arg Ser Lys Lys Val
 1340 1345 1350
 Ser Asn Cys Asn Leu Tyr Arg Leu Gly Lys Lys Lys Gly Leu Pro
 1355 1360 1365
 Ser Arg Met Val Val Ser Ile Phe Asp Pro Pro Val Asn Trp Leu
 1370 1375 1380
 Pro Pro Gly Tyr Val Val Asn Gln Asp Lys Ser Asn Thr Asp Lys
 1385 1390 1395
 Trp Glu Lys Asp Glu Met Thr Lys Asp Cys Met Leu Ala Asn Gly
 1400 1405 1410
 Lys Leu Asp Glu Asp Tyr Glu Glu Asp Glu Glu Glu Ser
 1415 1420 1425
 Leu Met Trp Arg Ala Pro Lys Glu Glu Ala Asp Tyr Glu Asp Asp
 1430 1435 1440
 Phe Leu Glu Tyr Asp Gln Glu His Ile Arg Phe Ile Asp Asn Met
 1445 1450 1455
 Leu Met Gly Ser Gly Ala Phe Val Lys Lys Ile Ser Leu Ser Pro
 1460 1465 1470
 Phe Ser Thr Thr Asp Ser Ala Tyr Glu Trp Lys Met Pro Lys Lys
 1475 1480 1485
 Ser Ser Leu Gly Ser Met Pro Phe Ser Ser Asp Phe Glu Asp Phe
 1490 1495 1500
 Asp Tyr Ser Ser Trp Asp Ala Met Cys Tyr Leu Asp Pro Ser Lys
 1505 1510 1515
 Ala Val Glu Glu Asp Asp Phe Val Val Gly Phe Trp Asn Pro Ser
 1520 1525 1530
 Glu Glu Asn Cys Gly Val Asp Thr Gly Lys Gln Ser Ile Ser Tyr
 1535 1540 1545
 Asp Leu His Thr Glu Gln Cys Ile Ala Asp Lys Ser Ile Ala Asp
 1550 1555 1560
 Cys Val Glu Ala Leu Leu Gly Cys Tyr Leu Thr Ser Cys Gly Glu
 1565 1570 1575
 Arg Ala Ala Gln Leu Phe Leu Cys Ser Leu Gly Leu Lys Val Leu
 1580 1585 1590
 Pro Val Ile Lys Arg Thr Asp Arg Glu Lys Ala Leu Cys Pro Thr
 1595 1600 1605
 Arg Glu Asn Phe Asn Ser Gln Gln Lys Asn Leu Ser Val Ser Cys
 1610 1615 1620
 Ala Ala Ser Val Ala Ser Ser Arg Ser Ser Val Leu Lys Asp
 1625 1630 1635

Ser Glu Tyr Gly Cys Leu Lys Ile Pro Pro Arg Cys Met Phe Asp
 1640 1645 1650
 His Pro Asp Ala Asp Lys Thr Leu Asn His Leu Ile Ser Gly Phe
 1655 1660 1665
 Glu Asn Phe Glu Lys Lys Ile Asn Tyr Arg Phe Lys Asn Lys Ala
 1670 1675 1680
 Tyr Leu Leu Gln Ala Phe Thr His Ala Ser Tyr His Tyr Asn Thr
 1685 1690 1695
 Ile Thr Asp Cys Tyr Gln Arg Leu Glu Phe Leu Gly Asp Ala Ile
 1700 1705 1710
 Leu Asp Tyr Leu Ile Thr Lys His Leu Tyr Glu Asp Pro Arg Gln
 1715 1720 1725
 His Ser Pro Gly Val Leu Thr Asp Leu Arg Ser Ala Leu Val Asn
 1730 1735 1740
 Asn Thr Ile Phe Ala Ser Leu Ala Val Lys Tyr Asp Tyr His Lys
 1745 1750 1755
 Tyr Phe Lys Ala Val Ser Pro Glu Leu Phe His Val Ile Asp Asp
 1760 1765 1770
 Phe Val Gln Phe Gln Leu Glu Lys Asn Glu Met Gln Gly Met Asp
 1775 1780 1785
 Ser Glu Leu Arg Arg Ser Glu Glu Asp Glu Glu Lys Glu Glu Asp
 1790 1795 1800
 Ile Glu Val Pro Lys Ala Met Gly Asp Ile Phe Glu Ser Leu Ala
 1805 1810 1815
 Gly Ala Ile Tyr Met Asp Ser Gly Met Ser Leu Glu Thr Val Trp
 1820 1825 1830
 Gln Val Tyr Tyr Pro Met Met Arg Pro Leu Ile Glu Lys Phe Ser
 1835 1840 1845
 Ala Asn Val Pro Arg Ser Pro Val Arg Glu Leu Leu Glu Met Glu
 1850 1855 1860
 Pro Glu Thr Ala Lys Phe Ser Pro Ala Glu Arg Thr Tyr Asp Gly
 1865 1870 1875
 Lys Val Arg Val Thr Val Glu Val Val Gly Lys Gly Lys Phe Lys
 1880 1885 1890
 Gly Val Gly Arg Ser Tyr Arg Ile Ala Lys Ser Ala Ala Ala Arg
 1895 1900 1905
 Arg Ala Leu Arg Ser Leu Lys Ala Asn Gln Pro Gln Val Pro Asn
 1910 1915 1920
 Ser

<210> 165
 <211> 482

<212> PRT
<213> Homo sapiens

<400> 165
Met Ala Gln Thr Gln Gly Thr Arg Arg Lys Val Cys Tyr Tyr Tyr Asp
1 5 10 15
Gly Asp Val Gly Asn Tyr Tyr Tyr Gly Gln Gly His Pro Met Lys Pro
20 25 30
His Arg Ile Arg Met Thr His Asn Leu Leu Asn Tyr Gly Leu Tyr
35 40 45
Arg Lys Met Glu Ile Tyr Arg Pro His Lys Ala Asn Ala Glu Glu Met
50 55 60
Thr Lys Tyr His Ser Asp Asp Tyr Ile Lys Phe Leu Arg Ser Ile Arg
65 70 75 80
Pro Asp Asn Met Ser Glu Tyr Ser Lys Gln Met Gln Arg Phe Asn Val
85 90 95
Gly Glu Asp Cys Pro Val Phe Asp Gly Leu Phe Glu Phe Cys Gln Leu
100 105 110
Ser Thr Gly Gly Ser Val Ala Ser Ala Val Lys Leu Asn Lys Gln Gln
115 120 125
Thr Asp Ile Ala Val Asn Trp Ala Gly Gly Leu His Ala Lys Lys
130 135 140
Ser Glu Ala Ser Gly Phe Cys Tyr Val Asn Asp Ile Val Leu Ala Ile
145 150 155 160
Leu Glu Leu Lys Tyr His Gln Arg Val Leu Tyr Ile Asp Ile Asp
165 170 175
Ile His His Gly Asp Gly Val Glu Glu Ala Phe Tyr Thr Thr Asp Arg
180 185 190
Val Met Thr Val Ser Phe His Lys Tyr Gly Glu Tyr Phe Pro Gly Thr
195 200 205
Gly Asp Leu Arg Asp Ile Gly Ala Gly Lys Gly Lys Tyr Tyr Ala Val
210 215 220
Asn Tyr Pro Leu Arg Asp Gly Ile Asp Asp Glu Ser Tyr Glu Ala Ile
225 230 235 240
Phe Lys Pro Val Met Ser Lys Val Met Glu Met Phe Gln Pro Ser Ala
245 250 255
Val Val Leu Gln Cys Gly Ser Asp Ser Leu Ser Gly Asp Arg Leu Gly
260 265 270
Cys Phe Asn Leu Thr Ile Lys Gly His Ala Lys Cys Val Glu Phe Val
275 280 285
Lys Ser Phe Asn Leu Pro Met Leu Met Leu Gly Gly Gly Tyr Thr
290 295 300
Ile Arg Asn Val Ala Arg Cys Trp Thr Tyr Glu Thr Ala Val Ala Leu

328

305 310 315 320
Asp Thr Glu Ile Pro Asn Glu Leu Pro Tyr Asn Asp Tyr Phe Glu Tyr
325 330 335
Phe Gly Pro Asp Phe Lys Leu His Ile Ser Pro Ser Asn Met Thr Asn
340 345 350
Gln Asn Thr Asn Glu Tyr Leu Glu Lys Ile Lys Gln Arg Leu Phe Glu
355 360 365
Asn Leu Arg Met Leu Pro His Ala Pro Gly Val Gln Met Gln Ala Ile
370 375 380
Pro Glu Asp Ala Ile Pro Glu Glu Ser Gly Asp Glu Asp Glu Asp Asp
385 390 395 400
Pro Asp Lys Arg Ile Ser Ile Cys Ser Ser Asp Lys Arg Ile Ala Cys
405 410 415
Glu Glu Glu Phe Ser Asp Ser Glu Glu Gly Glu Gly Arg Lys
420 425 430
Asn Ser Ser Asn Phe Lys Lys Ala Lys Arg Val Lys Thr Glu Asp Glu
435 440 445
Lys Glu Lys Asp Pro Glu Glu Lys Lys Glu Val Thr Glu Glu Lys
450 455 460
Thr Lys Glu Glu Lys Pro Glu Ala Lys Gly Val Lys Glu Val Lys
465 470 475 480
Leu Ala
<210> 166
<211> 556
<212> PRT
<213> Homo sapiens
<400> 166
Phe Arg Ala Phe Gly Thr Ser Ala Gly Trp Tyr Arg Ala Phe Pro Ala
1 5 10 15
Pro Pro Pro Leu Leu Pro Pro Ala Cys Pro Ser Pro Arg Asp Tyr Arg
20 25 30
Pro His Val Ser Leu Ser Pro Phe Leu Ser Arg Pro Ser Arg Gly Gly
35 40 45
Ser Ser Ser Ser Ser Arg Arg Arg Ser Pro Val Ala Ala Val
50 55 60
Ala Gly Glu Pro Met Ala Tyr Ser Gln Gly Gly Lys Lys Val
65 70 75 80
Cys Tyr Tyr Tyr Asp Gly Asp Ile Gly Asn Tyr Tyr Tyr Gly Gln Gly
85 90 95
His Pro Met Lys Pro His Arg Ile Arg Met Thr His Asn Leu Leu
100 105 110

329

Asn Tyr Gly Leu Tyr Arg Lys Met Glu Ile Tyr Arg Pro His Lys Ala
 115 120 125
 Thr Ala Glu Glu Met Thr Lys Tyr His Ser Asp Glu Tyr Ile Lys Phe
 130 135 140 145
 Leu Arg Ser Ile Arg Pro Asp Asn Met Ser Glu Tyr Ser Lys Glu Met
 145 150 155 160
 His Thr Val Asn Val Gly Glu Asp Cys Pro Val Phe Asp Gly Leu Phe
 165 170 175
 Glu Phe Cys Glu Leu Ser Thr Gly Ser Val Ala Gly Ala Val Lys
 180 185 190
 Leu Asn Arg Glu Glu Thr Asp Met Ala Val Asn Trp Ala Gly Gly Leu
 195 200 205
 His His Ala Lys Lys Ser Glu Ala Ser Gly Phe Cys Tyr Val Asn Asp
 210 215 220
 Ile Val Leu Ala Ile Leu Glu Leu Leu Lys Tyr His Glu Arg Val Leu
 225 230 235
 Tyr Ile Asp Ile Asp Ile His His Gly Asp Gly Val Glu Glu Ala Phe
 240 245 250 255
 Tyr Thr Thr Asp Arg Val Met Thr Val Ser Phe His Lys Tyr Gly Glu
 260 265 270
 Tyr Phe Pro Gly Thr Gly Asp Leu Arg Asp Ile Gly Ala Gly Lys Gly
 275 280 285
 Lys Tyr Tyr Ala Val Asn Phe Pro Met Arg Asp Gly Ile Asp Asp Glu
 290 295 300
 Ser Tyr Gly Glu Ile Phe Lys Pro Ile Ile Ser Lys Val Met Glu Met
 305 310 315 320
 Tyr Glu Pro Ser Ala Val Val Leu Glu Cys Gly Ala Asp Ser Leu Ser
 325 330 335
 Gly Asp Arg Leu Gly Cys Phe Asn Leu Thr Val Lys Gly His Ala Lys
 340 345 350
 Cys Val Glu Val Val Lys Thr Phe Asn Leu Pro Leu Leu Met Leu Gly
 355 360 365
 Gly Gly Gly Tyr Thr Ile Arg Asn Val Ala Arg Cys Trp Thr Tyr Glu
 370 375 380
 Thr Ala Val Ala Leu Asp Cys Glu Ile Pro Asn Glu Leu Pro Tyr Asn
 385 390 395 400
 Asp Tyr Phe Glu Tyr Phe Gly Pro Asp Phe Lys Leu His Ile Ser Pro
 405 410 415
 Ser Asn Met Thr Asn Glu Asn Thr Pro Glu Tyr Met Glu Lys Ile Lys
 420 425 430
 Glu Arg Leu Phe Glu Asn Leu Arg Met Leu Pro His Ala Pro Gly Val
 435 440 445

330

Gln Met Glu Ala Ile Pro Glu Asp Ala Val His Glu Asp Ser Gly Asp
 450 455 460
 Glu Asp Gly Glu Asp Pro Asp Lys Arg Ile Ser Ile Arg Ala Ser Asp
 465 470 475 480
 Lys Arg Ile Ala Cys Asp Glu Glu Phe Ser Asp Ser Glu Asp Glu Gly
 485 490 495
 Glu Gly Gly Arg Arg Asn Val Ala Asp His Lys Lys Gly Ala Lys Lys
 500 505 510
 Ala Arg Ile Glu Glu Asp Lys Lys Glu Thr Glu Asp Lys Lys Thr Asp
 515 520 525
 Val Lys Glu Glu Asp Lys Ser Lys Asp Asn Ser Gly Glu Lys Thr Asp
 530 535 540
 Thr Lys Gly Thr Lys Ser Glu Glu Leu Ser Asn Pro
 545 550 555
 <210> 167
 <211> 428
 <212> PRT
 <213> Homo sapiens
 <400> 167
 Met Ala Lys Thr Val Ala Tyr Phe Tyr Asp Pro Asp Val Gly Asn Phe
 1 5 10 15
 His Tyr Gly Ala Gly His Pro Met Lys Pro His Arg Leu Ala Leu Thr
 20 25 30
 His Ser Leu Val Leu His Tyr Gly Leu Tyr Lys Lys Met Ile Val Phe
 35 40 45
 Lys Pro Tyr Glu Ala Ser Glu His Asp Met Cys Arg Phe His Ser Glu
 50 55 60
 Asp Tyr Ile Asp Phe Leu Glu Arg Val Ser Pro Thr Asn Met Glu Gly
 65 70 75 80
 Phe Thr Lys Ser Leu Asn Ala Phe Asn Val Gly Asp Asp Cys Pro Val
 85 90 95
 Phe Pro Gly Leu Phe Glu Phe Cys Ser Arg Tyr Thr Gly Ala Ser Leu
 100 105 110
 Gln Gly Ala Thr Glu Leu Asn Asn Lys Ile Cys Asp Ile Ala Ile Asn
 115 120 125
 Trp Ala Gly Gly Leu His His Ala Lys Lys Phe Glu Ala Ser Gly Phe
 130 135 140
 Cys Tyr Val Asn Asp Ile Val Ile Gly Ile Leu Glu Leu Lys Tyr
 145 150 155 160
 His Pro Arg Val Leu Tyr Ile Asp Ile Asp Ile His His Gly Asp Gly
 165 170 175
 Val Glu Glu Ala Phe Tyr Leu Thr Asp Arg Val Met Thr Val Ser Phe

331

180 185 190
 His Lys Tyr Gly Asn Tyr Phe Pro Gly Thr Gly Asp Met Tyr Glu 205
 195 200
 Val Gly Ala Glu Ser Gly Arg Tyr Tyr Cys Leu Asn Val Pro Leu Arg 220
 210 215
 Asp Gly Ile Asp Asp Gln Ser Tyr Lys His Leu Phe Gln Pro Val Ile 240
 225 230 235
 Asn Gln Val Val Asp Phe Tyr Gln Pro Thr Cys Ile Val Leu Gln Cys 255
 245 250
 Gly Ala Asp Ser Leu Gly Cys Asp Arg Leu Gly Cys Phe Asn Leu Ser 270
 260 265
 Ile Arg Gly His Gly Glu Cys Val Glu Tyr Val Lys Ser Phe Asn Ile 285
 275 280
 Pro Leu Leu Val Leu Gly Gly Gly Tyr Thr Val Arg Asn Val Ala 300
 290 295
 Arg Cys Trp Thr Tyr Glu Thr Ser Leu Leu Val Glu Ala Ile Ser 320
 305 310 315
 Glu Glu Leu Pro Tyr Ser Glu Tyr Phe Glu Tyr Phe Ala Pro Asp Phe 335
 325 330
 Thr Leu His Pro Asp Val Ser Thr Arg Ile Glu Asn Gln Asn Ser Arg 350
 340 345
 Gln Tyr Leu Asp Gln Ile Arg Gln Thr Ile Phe Glu Asn Leu Lys Met 365
 355 360
 Leu Asn His Ala Pro Ser Val Gln Ile His Asp Val Pro Ala Asp Leu 380
 370 375
 Leu Thr Tyr Asp Arg Thr Asp Glu Ala Asp Ala Glu Glu Arg Gly Pro 400
 385 390 395
 Glu Glu Asn Tyr Ser Arg Pro Glu Ala Pro Asn Glu Phe Tyr Asp Gly 415
 405 410
 Asp His Asp Asn Asp Lys Glu Ser Asp Val Glu Ile 425
 420 425
 <210> 168
 <211> 450
 <212> PRT
 <213> Homo sapiens
 <400> 168
 Met Ser Ala Ile Gln Ala Ala Trp Pro Ser Gly Thr Glu Cys Ile Ala 15
 1 5 10
 Lys Tyr Asn Phe His Gly Thr Ala Glu Gln Asp Leu Pro Phe Cys Lys 30
 20 25
 Gly Asp Val Leu Thr Ile Val Ala Val Thr Lys Asp Pro Asn Trp Tyr 45
 35 40

332

Lys Ala Lys Asn Lys Val Gly Arg Glu Gly Ile Ile Pro Ala Asn Tyr 55
 50 60
 Val Gln Lys Arg Glu Gly Val Lys Ala Gly Thr Lys Leu Ser Leu Met 80
 65 70 75
 Pro Trp Phe His Gly Lys Ile Thr Arg Glu Gln Ala Glu Arg Leu Leu 95
 85 90
 Tyr Pro Pro Glu Thr Gly Leu Phe Leu Val Arg Glu Ser Thr Asn Tyr 110
 100 105
 Pro Gly Asp Tyr Thr Leu Cys Val Ser Cys Asp Gly Lys Val Glu His 125
 115 120
 Tyr Arg Ile Met Tyr His Ala Ser Lys Leu Ser Ile Asp Glu Glu Val 140
 130 135
 Tyr Phe Glu Asn Leu Met Gln Leu Val Glu His Tyr Thr Ser Asp Ala 160
 145 150 155
 Asp Gly Leu Cys Thr Arg Leu Ile Lys Pro Lys Val Met Glu Gly Thr 175
 165 170
 Val Ala Ala Gln Asp Glu Phe Tyr Arg Ser Gly Trp Ala Leu Asn Met 190
 180 185
 Lys Glu Leu Lys Leu Leu Gln Thr Ile Gly Lys Gly Glu Phe Gly Asp 205
 195 200
 Val Met Leu Gly Asp Tyr Arg Gly Asn Lys Val Ala Val Lys Cys Ile 220
 210 215
 Lys Asn Asp Ala Thr Ala Gln Ala Phe Leu Ala Glu Ala Ser Val Met 240
 225 230 235
 Thr Gln Leu Arg His Ser Asn Leu Val Gln Leu Leu Gly Val Ile Val 255
 245 250
 Glu Glu Lys Gly Glu Leu Tyr Ile Val Thr Glu Tyr Met Ala Lys Gly 270
 260 265
 Ser Leu Val Asp Tyr Leu Arg Ser Arg Gly Arg Ser Val Leu Gly Gly 285
 275 280
 Asp Cys Leu Leu Lys Phe Ser Leu Asp Val Cys Glu Ala Met Glu Tyr 300
 290 295
 Leu Glu Gly Asn Asn Phe Val His Arg Asp Leu Ala Ala Arg Asn Val 320
 305 310 315
 Leu Val Ser Glu Asp Asn Val Ala Lys Val Ser Asp Phe Gly Leu Thr 335
 325 330
 Lys Glu Ala Ser Ser Thr Gln Asp Thr Gly Lys Leu Pro Val Lys Trp 350
 340 345
 Thr Ala Pro Glu Ala Leu Arg Glu Lys Lys Phe Ser Thr Lys Ser Asp 365
 355 360
 Val Trp Ser Phe Gly Ile Leu Leu Trp Glu Ile Tyr Ser Phe Gly Arg 380
 370 375

333

Val Pro Tyr Pro Arg Ile Pro Leu Lys Asp Val Val Pro Arg Val Glu
385 390 395 400
Lys Gly Tyr Lys Met Asp Ala Pro Asp Gly Cys Pro Pro Ala Val Tyr
405 410 415
Glu Val Met Lys Asn Cys Trp His Leu Asp Ala Ala Met Arg Pro Ser
420 425 430
Phe Leu Gln Leu Arg Glu Gln Leu His Ile Lys Thr His Glu Leu
435 440 445
His Leu
450
<210> 169
<211> 507
<212> PRT
<213> Homo sapiens
<400> 169
Met Ala Gly Arg Gly Ser Leu Val Ser Trp Arg Ala Phe His Gly Cys
1 5 10 15
Asp Ser Ala Glu Glu Leu Pro Arg Val Ser Pro Arg Phe Leu Arg Ala
20 25 30
Trp His Pro Pro Val Ser Ala Arg Met Pro Thr Arg Arg Trp Ala
35 40 45
Pro Gly Thr Gln Cys Ile Thr Lys Cys Glu His Thr Arg Pro Lys Pro
50 55 60
Gly Glu Leu Ala Phe Arg Lys Gly Asp Val Val Thr Ile Leu Glu Ala
65 70 75 80
Cys Glu Asn Lys Ser Trp Tyr Arg Val Lys His His Thr Ser Gly Gln
85 90 95
Glu Gly Leu Leu Ala Ala Gly Ala Leu Arg Glu Arg Glu Ala Leu Ser
100 105 110
Ala Asp Pro Lys Leu Ser Leu Met Pro Trp Phe His Gly Lys Ile Ser
115 120 125
Gly Gln Glu Ala Val Gln Gln Leu Gln Pro Pro Glu Asp Gly Leu Phe
130 135 140
Leu Val Arg Glu Ser Ala Arg His Pro Gly Asp Tyr Val Leu Cys Val
145 150 155 160
Ser Phe Gly Arg Asp Val Ile His Tyr Arg Val Leu His Arg Asp Gly
165 170 175
His Leu Thr Ile Asp Glu Ala Val Phe Phe Cys Asn Leu Met Asp Met
180 185 190
Val Glu His Tyr Ser Lys Asp Lys Gly Ala Ile Cys Thr Lys Leu Val
195 200 205
Arg Pro Lys Arg Lys His Gly Thr Lys Ser Ala Glu Glu Leu Ala

334

210 215 220
Arg Ala Gly Trp Leu Asn Leu Gln His Leu Thr Leu Gly Ala Gln
225 230 235 240
Ile Gly Glu Gly Glu Phe Gly Ala Val Leu Gln Gly Glu Tyr Leu Gly
245 250 255
Gln Lys Val Ala Val Lys Asn Ile Lys Cys Asp Val Thr Ala Gln Ala
260 265 270
Phe Leu Asp Glu Thr Ala Val Met Thr Lys Met Gln His Glu Asn Leu
275 280 285
Val Arg Leu Leu Gly Val Ile Leu His Gln Gly Leu Tyr Ile Val Met
290 295 300
Glu His Val Ser Lys Gly Asn Leu Val Asn Phe Leu Arg Thr Arg Gly
305 310 315 320
Arg Ala Leu Val Asn Thr Ala Gln Leu Leu Gln Phe Ser Leu His Val
325 330 335
Ala Glu Gly Met Glu Tyr Leu Glu Ser Lys Lys Leu Val His Arg Asp
340 345 350
Leu Ala Ala Arg Asn Ile Leu Val Ser Glu Asp Leu Val Ala Lys Val
355 360 365
Ser Asp Phe Gly Leu Ala Lys Ala Glu Arg Lys Gly Leu Asp Ser Ser
370 375 380
Arg Leu Pro Val Lys Trp Thr Ala Pro Glu Ala Leu Lys His Gly Lys
385 390 395 400
Phe Thr Ser Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu
405 410 415
Val Phe Ser Tyr Gly Arg Ala Pro Tyr Pro Lys Met Ser Leu Lys Glu
420 425 430
Val Ser Glu Ala Val Glu Lys Gly Tyr Arg Met Glu Pro Pro Glu Gly
435 440 445
Cys Pro Gly Pro Val His Val Leu Met Ser Ser Cys Trp Glu Ala Glu
450 455 460
Pro Ala Arg Arg Pro Pro Phe Arg Lys Leu Ala Glu Lys Leu Ala Arg
465 470 475 480
Glu Leu Arg Ser Ala Gly Ala Pro Ala Ser Val Ser Gly Gln Asp Ala
485 490 495
Asp Gly Ser Thr Ser Pro Arg Ser Gln Glu Pro
500 505
<210> 170
<211> 1332
<212> PRT
<213> Homo sapiens
<400> 170

335

Met Arg Asn Leu Lys Leu Phe Arg Thr Leu Glu Phe Arg Asp Ile Gln
1 10 15
Gly Pro Gly Asn Pro Gln Cys Phe Ser Leu Arg Thr Glu Gln Gly Thr
20 25 30
Val Leu Ile Gly Ser Glu His Gly Leu Ile Glu Val Asp Pro Val Ser
35 40 45
Arg Glu Val Lys Asn Glu Val Ser Leu Val Ala Glu Gly Phe Leu Pro
50 55 60
Glu Asp Gly Ser Gly Arg Ile Val Gly Val Gln Asp Leu Leu Asp Gln
65 70 75 80
Glu Ser Val Cys Val Ala Thr Ala Ser Gly Asp Val Ile Leu Cys Ser
85 90 95
Leu Ser Thr Gln Gln Leu Glu Cys Val Gly Ser Val Ala Ser Gly Ile
100 105 110
Ser Val Met Ser Trp Ser Pro Asp Gln Glu Leu Val Leu Leu Ala Thr
115 120 125
Gly Gln Gln Thr Leu Ile Met Met Thr Lys Asp Phe Glu Pro Ile Leu
130 135 140
Glu Gln Gln Ile His Gln Asp Asp Phe Gly Glu Ser Lys Phe Ile Thr
145 150 155 160
Val Gly Trp Gly Arg Lys Glu Thr Gln Phe His Gly Ser Glu Gly Arg
165 170 175
Gln Ala Ala Phe Gln Met Gln Met His Glu Ser Ala Leu Pro Trp Asp
180 185 190
Asp His Arg Pro Gln Val Thr Trp Arg Gly Asp Gly Gln Phe Ala
195 200 205
Val Ser Val Val Cys Pro Glu Thr Gly Ala Arg Lys Val Arg Val Trp
210 215 220
Asn Arg Glu Phe Ala Leu Gln Ser Thr Ser Glu Pro Val Ala Gly Leu
225 230 235 240
Gly Pro Ala Leu Ala Trp Lys Pro Ser Gly Ser Leu Ile Ala Ser Thr
245 250 255
Gln Asp Lys Pro Asn Gln Gln Asp Ile Val Phe Phe Glu Lys Asn Gly
260 265 270
Leu Leu His Gly His Phe Thr Leu Pro Phe Leu Lys Asp Glu Val Lys
275 280 285
Val Asn Asp Leu Leu Trp Asn Ala Asp Ser Ser Val Leu Ala Val Trp
290 295 300
Leu Glu Asp Leu Gln Arg Glu Glu Ser Ile Pro Lys Thr Cys Val
305 310 315 320
Gln Leu Trp Thr Val Gly Asn Tyr His Trp Tyr Leu Lys Gln Ser Leu
325 330 335

336

Ser Phe Ser Thr Cys Gly Lys Ser Lys Ile Val Ser Leu Met Trp Asp
340 345 350
Pro Val Thr Pro Tyr Arg Leu His Val Leu Cys Gln Gly Trp His Tyr
355 360 365
Leu Ala Tyr Asp Trp His Trp Thr Thr Asp Arg Ser Val Gly Asp Asn
370 375 380
Ser Ser Asp Leu Ser Asn Val Ala Val Ile Asp Gly Asn Arg Val Leu
385 390 395 400
Val Thr Val Phe Arg Gln Thr Val Val Pro Pro Met Cys Thr Tyr
405 410 415
Gln Leu Leu Phe Pro His Pro Val Asn Gln Val Thr Phe Leu Ala His
420 425 430
Pro Gln Lys Ser Asn Asp Leu Ala Val Leu Asp Ala Ser Asn Gln Ile
435 440 445
Ser Val Tyr Lys Cys Gly Asp Cys Pro Ser Ala Asp Pro Thr Val Lys
450 455 460
Leu Gly Ala Val Gly Gly Ser Gly Phe Lys Val Cys Leu Arg Thr Pro
465 470 475 480
His Leu Glu Lys Arg Tyr Lys Ile Gln Phe Glu Asn Asn Glu Asp Gln
485 490 495
Asp Val Asn Pro Leu Lys Leu Gly Leu Leu Thr Trp Ile Glu Glu Asp
500 505 510
Val Phe Leu Ala Val Ser His Ser Glu Phe Ser Pro Arg Ser Val Ile
515 520 525
His His Leu Thr Ala Ala Ser Ser Glu Met Asp Glu Glu His Gly Gln
530 535 540
Leu Asn Val Ser Ser Ser Ala Ala Val Asp Gly Val Ile Ile Ser Leu
545 550 555 560
Cys Cys Asn Ser Lys Thr Lys Ser Val Val Leu Gln Leu Ala Asp Gly
565 570 575
Gln Ile Phe Lys Tyr Leu Trp Glu Ser Pro Ser Leu Ala Ile Lys Pro
580 585 590
Trp Lys Asn Ser Gly Gly Phe Pro Val Arg Phe Pro Tyr Pro Cys Thr
595 600 605
Gln Thr Glu Leu Ala Met Ile Gly Glu Glu Glu Cys Val Leu Gly Leu
610 615 620
Thr Asp Arg Cys Arg Phe Phe Ile Asn Asp Ile Glu Val Ala Ser Asn
625 630 635 640
Ile Thr Ser Phe Ala Val Tyr Asp Glu Phe Leu Leu Thr Thr His
645 650 655
Ser His Thr Cys Gln Cys Phe Cys Leu Arg Asp Ala Ser Phe Lys Thr

337

Leu Gln Ala Gly Leu Ser Ser Asn His Val Ser His Gly Glu Val Leu 670
 660 665 680 685
 Arg Lys Val Glu Arg Gly Ser Arg Ile Val Thr Val Val Pro Gln Asp 700
 690 695
 Thr Lys Leu Val Leu Gln Met Pro Arg Gly Asn Leu Glu Val Val His 715
 705 710 720
 His Arg Ala Leu Val Leu Ala Gln Ile Arg Lys Trp Leu Asp Lys Leu 730
 725 735
 Met Phe Lys Glu Ala Phe Glu Cys Met Arg Lys Leu Arg Ile Asn Leu 745
 740 750
 Asn Leu Ile Tyr Asp His Asn Pro Lys Val Phe Leu Gly Asn Val Glu 760
 755 765
 Thr Phe Ile Lys Gln Ile Asp Ser Val Asn His Ile Asn Leu Phe Phe 775
 770 780
 Thr Glu Leu Lys Glu Asp Val Thr Lys Thr Met Tyr Pro Ala Pro 795
 785 800
 Val Thr Ser Ser Val Tyr Leu Ser Arg Asp Pro Asp Gly Asn Lys Ile 810
 805 815
 Asp Leu Val Cys Asp Ala Met Arg Ala Val Met Glu Ser Ile Asn Pro 825
 820 830
 His Lys Tyr Cys Leu Ser Ile Leu Thr Ser His Val Lys Lys Thr Thr 840
 835 845
 Pro Glu Leu Glu Ile Val Leu Gln Lys Val His Glu Leu Gln Gly Asn 855
 850 860
 Ala Pro Ser Asp Pro Asp Ala Val Ser Ala Glu Glu Ala Leu Lys Tyr 875
 865 880
 Leu Leu His Leu Val Asp Val Asn Glu Leu Tyr Asp His Ser Leu Gly 890
 885 895
 Thr Tyr Asp Phe Asp Leu Val Leu Met Val Ala Glu Lys Ser Gln Lys 905
 900 910
 Asp Pro Lys Glu Tyr Leu Pro Phe Leu Asn Thr Leu Lys Lys Met Glu 920
 915 925
 Thr Asn Tyr Gln Arg Phe Thr Ile Asp Lys Tyr Leu Lys Arg Tyr Glu 935
 930 940
 Lys Ala Ile Gly His Leu Ser Lys Cys Gly Pro Glu Tyr Phe Pro Glu 955
 945 960
 Cys Leu Asn Leu Ile Lys Asp Lys Asn Leu Tyr Asn Glu Ala Leu Lys 970
 965 975
 Leu Tyr Ser Pro Ser Ser Gln Gln Tyr Gln Asp Ile Ser Ile Ala Tyr 985
 980 990

Gly Glu His Leu Met Gln Glu His Met Tyr Glu Pro Ala Gly Leu Met 1000
 995 1005
 Phe Ala Arg Cys Gly Ala His Glu Lys Ala Leu Ser Ala Phe Leu 1015
 1010 1020
 Thr Cys Gly Asn Trp Lys Gln Ala Leu Cys Val Ala Ala Gln Leu 1030
 1025 1035
 Asn Phe Thr Lys Asp Gln Leu Val Gly Leu Gly Arg Thr Leu Ala 1045
 1040 1050
 Gly Lys Leu Val Glu Gln Arg Lys His Ile Asp Ala Ala Met Val 1060
 1055 1065
 Leu Glu Glu Ser Ala Gln Asp Tyr Glu Glu Ala Val Leu Leu Leu 1075
 1070 1080
 Leu Glu Gly Ala Ala Trp Glu Glu Ala Leu Arg Leu Val Tyr Lys 1090
 1085 1095
 Tyr Asn Arg Leu Asp Ile Ile Glu Thr Asn Val Lys Pro Ser Ile 1105
 1100 1110
 Leu Glu Ala Gln Lys Asn Tyr Met Ala Phe Leu Asp Ser Gln Thr 1120
 1115 1125
 Ala Thr Phe Ser Arg His Lys Lys Arg Leu Leu Val Val Arg Glu 1135
 1130 1140
 Leu Lys Glu Gln Ala Gln Gln Ala Gly Leu Asp Asp Glu Val Pro 1150
 1145 1155
 His Gly Gln Glu Ser Asp Leu Phe Ser Glu Thr Ser Ser Val Val 1165
 1160 1170
 Ser Gly Ser Glu Met Ser Gly Lys Tyr Ser His Ser Asn Ser Arg 1180
 1175 1185
 Ile Ser Ala Arg Ser Ser Lys Asn Arg Arg Lys Ala Glu Arg Lys 1195
 1190 1200
 Lys His Ser Leu Lys Glu Gly Ser Pro Leu Glu Asp Leu Ala Leu 1210
 1205 1215
 Leu Glu Ala Leu Ser Glu Val Val Gln Asn Thr Glu Asn Leu Lys 1225
 1220 1230
 Asp Glu Val Tyr His Ile Leu Lys Val Leu Phe Leu Phe Glu Phe 1240
 1235 1245
 Asp Glu Gln Gly Arg Glu Leu Gln Lys Ala Phe Glu Asp Thr Leu 1255
 1250 1260
 Gln Leu Met Glu Arg Ser Leu Pro Glu Ile Trp Thr Leu Thr Tyr 1270
 1265 1275
 Gln Gln Asn Ser Ala Thr Pro Val Leu Gly Pro Asn Ser Thr Ala 1285
 1280 1290
 Asn Ser Ile Met Ala Ser Tyr Gln Gln Gln Lys Thr Ser Val Pro 1300
 1295 1305

Val Leu Asp Ala Glu Leu Phe Ile Pro Pro Lys Ile Asn Arg Arg
1310 1315 1320

Thr Gln Trp Lys Leu Ser Leu Leu Asp
1325 1330

<210> 171
<211> 3371
<212> PRT
<213> Homo sapiens

<400> 171
Ser Ser Asp Ser Ser Ser Ser Ser Asp Asp Ser Pro Ala Arg Ser
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Val Gln Ser Ala Ala Val Pro Ala Pro Thr Ser Gln Leu Leu Ser Ser
20 25 30

Leu Glu Lys Asp Glu Pro Arg Lys Ser Phe Gly Ile Lys Val Gln Asn
35 40 45

Leu Pro Val Arg Ser Thr Asp Thr Ser Leu Lys Asp Gly Leu Phe His
50 55 60

Glu Phe Lys Lys Phe Gly Lys Val Thr Ser Val Gln Ile His Gly Thr
65 70 75 80

Ser Glu Glu Arg Tyr Gly Leu Val Phe Phe Arg Gln Gln Glu Asp Gln
85 90 95

Glu Lys Ala Leu Thr Ala Ser Lys Gly Lys Leu Phe Phe Gly Met Gln
100 105 110

Ile Glu Val Thr Ala Trp Ile Gly Pro Glu Thr Glu Ser Glu Asn Glu
115 120 125

Phe Arg Pro Leu Asp Glu Arg Ile Asp Glu Phe His Pro Lys Ala Thr
130 135 140

Arg Thr Leu Phe Ile Gly Asn Leu Glu Lys Thr Thr Thr Tyr His Asp
145 150 155 160

Leu Arg Asn Ile Phe Gln Arg Phe Gly Glu Ile Val Asp Ile Asp Ile
165 170 175

Lys Lys Val Asn Gly Val Pro Gln Tyr Ala Phe Leu Gln Tyr Cys Asp
180 185 190

Ile Ala Ser Val Cys Lys Ala Ile Lys Lys Met Asp Gly Glu Tyr Leu
195 200 205

Gly Asn Asn Arg Leu Lys Leu Gly Phe Gly Lys Ser Met Pro Thr Asn
210 215 220

Cys Val Trp Leu Asp Gly Leu Ser Ser Asn Val Ser Asp Gln Tyr Leu
225 230 235 240

Thr Arg His Phe Cys Arg Tyr Gly Pro Val Val Lys Val Phe Asp
245 250 255

Arg Leu Lys Gly Met Ala Leu Val Leu Tyr Asn Glu Ile Glu Tyr Ala

340

260 265 270

Gln Ala Ala Val Lys Glu Thr Lys Gly Arg Lys Ile Gly Gly Asn Lys
275 280 285

Ile Lys Val Asp Phe Ala Asn Arg Glu Ser Gln Leu Ala Phe Tyr His
290 295 300

Cys Met Glu Lys Ser Gly Gln Asp Ile Arg Asp Phe Tyr Glu Met Leu
305 310 315 320

Ala Glu Arg Arg Glu Glu Arg Arg Ala Ser Tyr Asp Tyr Asn Gln Asp
325 330 335

Arg Thr Tyr Tyr Glu Ser Val Arg Thr Pro Gly Thr Tyr Pro Glu Asp
340 345 350

Ser Arg Arg Asp Tyr Pro Ala Arg Gly Arg Glu Phe Tyr Ser Glu Trp
355 360 365

Glu Thr Tyr Gln Gly Asp Tyr Tyr Glu Ser Arg Tyr Tyr Asp Asp Pro
370 375 380

Arg Glu Tyr Arg Asp Tyr Arg Asn Asp Pro Tyr Glu Gln Asp Ile Arg
385 390 395 400

Glu Tyr Ser Tyr Arg Gln Arg Glu Arg Glu Arg Glu Arg Glu Arg Phe
405 410 415

Glu Ser Asp Arg Asp Arg Asp His Glu Arg Arg Pro Ile Glu Arg Ser
420 425 430

Gln Ser Pro Val His Leu Arg Arg Pro Gln Ser Pro Gly Ala Ser Pro
435 440 445

Ser Gln Ala Glu Arg Leu Pro Ser Asp Ser Glu Arg Arg Leu Tyr Ser
450 455 460

Arg Ser Ser Asp Arg Ser Gly Ser Cys Ser Ser Leu Ser Pro Pro Arg
465 470 475 480

Tyr Glu Lys Leu Asp Lys Ser Arg Leu Glu Arg Tyr Thr Lys Asn Glu
485 490 495

Lys Thr Asp Lys Glu Arg Thr Phe Asp Pro Glu Arg Val Glu Arg Glu
500 505 510

Arg Arg Leu Ile Arg Lys Glu Lys Val Glu Lys Asp Lys Thr Asp Lys
515 520 525

Gln Lys Arg Lys Gly Lys Val His Ser Pro Ser Ser Gln Ser Ser Glu
530 535 540

Thr Asp Gln Glu Asn Glu Arg Glu Gln Ser Pro Glu Lys Pro Arg Ser
545 550 555 560

Cys Asn Lys Leu Ser Arg Glu Lys Ala Asp Lys Glu Gly Ile Ala Lys
565 570 575

Asn Arg Leu Glu Leu Met Pro Cys Val Val Leu Thr Arg Val Lys Glu
580 585 590

341

Lys Glu Gly Lys Val Ile Asp His Thr Pro Val Glu Lys Leu Lys Ala
 595 600 605
 Lys Leu Asp Asn Asp Thr Val Lys Ser Ala Leu Asp Gln Lys Leu
 610 615 620
 Gln Val Ser Gln Thr Glu Pro Ala Lys Ser Asp Leu Ser Lys Leu Glu
 625 630 635 640
 Ser Val Arg Met Lys Val Pro Lys Glu Lys Gly Leu Ser Ser His Val
 645 650 655
 Glu Val Val Glu Lys Glu Gly Arg Leu Lys Ala Arg Lys His Leu Lys
 660 665 670
 Pro Glu Gln Pro Ala Asp Gly Val Ser Ala Val Asp Leu Glu Lys Leu
 675 680 685
 Glu Ala Arg Lys Arg Arg Phe Ala Asp Ser Asn Leu Lys Ala Glu Lys
 690 695 700
 Gln Lys Pro Glu Val Lys Lys Ser Ser Pro Glu Met Glu Asp Ala Arg
 705 710 715 720
 Val Leu Ser Lys Lys Gln Pro Asp Val Ser Ser Arg Glu Val Ile Leu
 725 730 735
 Leu Arg Glu Gly Glu Ala Glu Arg Lys Pro Val Arg Lys Glu Ile Leu
 740 745 750
 Lys Arg Glu Ser Lys Lys Ile Lys Leu Asp Arg Leu Asn Thr Val Ala
 755 760 765
 Ser Pro Lys Asp Cys Gln Glu Leu Ala Ser Ile Ser Val Gly Ser Gly
 770 775 780
 Ser Arg Pro Ser Ser Asp Leu Gln Ala Arg Leu Gly Glu Leu Ala Gly
 785 790 795 800
 Glu Ser Val Glu Asn Gln Glu Val Gln Ser Lys Lys Pro Ile Pro Ser
 805 810 815
 Lys Pro Gln Leu Lys Gln Leu Gln Val Leu Asp Asp Gln Gly Pro Glu
 820 825 830
 Arg Glu Asp Val Arg Lys Asn Tyr Cys Ser Leu Arg Asp Glu Thr Pro
 835 840 845
 Glu Arg Lys Ser Gly Gln Glu Lys Ser His Ser Val Asn Thr Glu Glu
 850 855 860
 Lys Ile Gly Ile Asp Ile Asp His Thr Gln Ser Tyr Arg Lys Gln Met
 865 870 875 880
 Glu Gln Ser Arg Arg Lys Gln Met Glu Met Glu Ile Ala Lys Ser
 885 890 895
 Glu Lys Phe Gly Ser Pro Lys Lys Asp Val Asp Glu Tyr Glu Arg Arg
 900 905 910
 Ser Leu Val His Glu Val Gly Lys Pro Pro Gln Asp Val Thr Asp Asp
 915 920 925

Ser Pro Pro Ser Lys Lys Lys Arg Met Asp His Val Asp Phe Asp Ile
 930 935 940
 Cys Thr Lys Arg Glu Arg Asn Tyr Arg Ser Ser Arg Gln Ile Ser Glu
 945 950 955 960
 Asp Ser Glu Arg Thr Gly Ser Pro Ser Val Arg His Gly Ser Phe
 965 970 975
 His Glu Asp Glu Asp Pro Ile Gly Ser Pro Arg Leu Ser Val Lys
 980 985 990
 Gly Ser Pro Lys Val Asp Glu Lys Val Leu Pro Tyr Ser Asn Ile Thr
 995 1000 1005
 Val Arg Glu Glu Ser Leu Lys Phe Asn Pro Tyr Asp Ser Ser Arg
 1010 1015 1020
 Arg Glu Gln Met Ala Asp Met Ala Lys Ile Lys Leu Ser Val Leu
 1025 1030 1035
 Asn Ser Glu Asp Glu Leu Asn Arg Trp Asp Ser Gln Met Lys Gln
 1040 1045 1050
 Asp Ala Gly Arg Phe Asp Val Ser Phe Pro Asn Ser Ile Ile Lys
 1055 1060 1065
 Arg Asp Ser Leu Arg Lys Arg Ser Val Arg Asp Leu Glu Pro Gly
 1070 1075 1080
 Glu Val Pro Ser Asp Ser Asp Glu Asp Gly Glu His Lys Ser His
 1085 1090 1095
 Ser Pro Arg Ala Ser Ala Leu Tyr Glu Ser Ser Arg Leu Ser Phe
 1100 1105 1110
 Leu Leu Arg Asp Arg Glu Asp Lys Leu Arg Glu Arg Asp Glu Arg
 1115 1120 1125
 Leu Ser Ser Ser Leu Glu Arg Asn Lys Phe Tyr Ser Phe Ala Leu
 1130 1135 1140
 Asp Lys Thr Ile Thr Pro Asp Thr Lys Ala Leu Leu Glu Arg Ala
 1145 1150 1155
 Lys Ser Leu Ser Ser Ser Arg Glu Glu Asn Trp Ser Phe Leu Asp
 1160 1165 1170
 Trp Asp Ser Arg Phe Ala Asn Phe Arg Asn Asn Lys Asp Lys Glu
 1175 1180 1185
 Lys Val Asp Ser Ala Pro Arg Pro Ile Pro Ser Trp Tyr Met Lys
 1190 1195 1200
 Lys Lys Lys Ile Arg Thr Asp Ser Glu Gly Lys Met Asp Asp Lys
 1205 1210 1215
 Lys Glu Asp His Lys Glu Glu Gln Glu Arg Gln Glu Leu Phe
 1220 1225 1230
 Ala Ser Arg Phe Leu His Ser Ser Ile Phe Glu Gln Asp Ser Lys

1235 1240 1245
 Arg Leu Gln His Leu Glu Arg Lys Glu Glu Asp Ser Asp Phe Ile 1260
 1250 1255
 Ser Gly Arg Ile Tyr Gly Lys Gln Thr Ser Glu Gly Ala Asn Ser 1275
 1265 1270 1275
 Thr Thr Asp Ser Ile Gln Glu Pro Val Val Leu Phe His Ser Arg 1290
 1280 1285 1290
 Phe Met Glu Leu Thr Arg Met Gln Gln Lys Glu Lys Asp 1305
 1295 1300 1305
 Gln Lys Pro Lys Glu Val Glu Lys Gln Glu Asp Thr Glu Asn His 1320
 1310 1315 1320
 Pro Lys Thr Pro Glu Ser Ala Pro Glu Asn Lys Asp Ser Glu Leu 1335
 1325 1330 1335
 Lys Thr Pro Pro Ser Val Gly Pro Pro Ser Val Thr Val Val Thr 1350
 1340 1345 1350
 Leu Glu Ser Ala Pro Ser Ala Leu Glu Lys Thr Thr Gly Asp Lys 1365
 1355 1360 1365
 Thr Val Glu Ala Pro Leu Val Thr Glu Glu Lys Thr Val Glu Pro 1380
 1370 1375 1380
 Ala Thr Val Ser Glu Glu Ala Lys Pro Ala Ser Glu Pro Ala Pro 1395
 1385 1390 1395
 Ala Pro Val Glu Gln Leu Glu Gln Val Asp Leu Pro Pro Gly Ala 1410
 1400 1405 1410
 Asp Pro Asp Lys Glu Ala Ala Met Met Pro Ala Gly Val Glu Glu 1425
 1415 1420 1425
 Gly Ser Ser Gly Asp Gln Pro Pro Tyr Leu Asp Ala Lys Pro Pro 1440
 1430 1435 1440
 Thr Pro Gly Ala Ser Phe Ser Gln Ala Glu Ser Asn Val Asp Pro 1455
 1445 1450 1455
 Glu Pro Asp Ser Thr Gln Pro Leu Ser Lys Pro Ala Gln Lys Ser 1470
 1460 1465 1470
 Glu Glu Ala Asn Glu Pro Lys Ala Glu Lys Pro Asp Ala Thr Ala 1485
 1475 1480 1485
 Asp Ala Glu Pro Asp Ala Asn Gln Lys Ala Glu Ala Ala Pro Glu 1500
 1490 1495 1500
 Ser Gln Pro Pro Ala Ser Glu Asp Leu Glu Val Asp Pro Pro Val 1515
 1505 1510 1515
 Ala Ala Lys Asp Lys Lys Pro Asn Lys Ser Lys Arg Ser Lys Thr 1530
 1520 1525 1530
 Pro Val Gln Ala Ala Val Ser Ile Val Glu Lys Pro Val Thr 1545
 1535 1540 1545

Arg Lys Ser Glu Arg Ile Asp Arg Glu Lys Leu Lys Arg Ser Asn 1550
 1555
 Ser Pro Arg Gly Glu Ala Gln Lys Leu Leu Glu Leu Lys Met Glu 1575
 1565 1570 1575
 Ala Glu Lys Ile Thr Arg Thr Ala Ser Lys Asn Ser Ala Ala Asp 1590
 1580 1585 1590
 Leu Glu His Pro Glu Pro Ser Leu Pro Leu Ser Arg Thr Arg Arg 1605
 1595 1600 1605
 Arg Asn Val Arg Ser Val Tyr Ala Thr Met Gly Asp His Glu Asn 1620
 1610 1615 1620
 Arg Ser Pro Val Lys Glu Pro Val Glu Gln Pro Arg Val Thr Arg 1635
 1625 1630 1635
 Lys Arg Leu Glu Arg Glu Leu Gln Glu Ala Ala Val Pro Thr 1650
 1640 1645 1650
 Thr Pro Arg Arg Gly Arg Pro Pro Lys Thr Arg Arg Arg Ala Asp 1665
 1655 1660 1665
 Glu Glu Glu Glu Asn Glu Ala Lys Glu Pro Ala Glu Thr Leu Lys 1680
 1670 1675 1680
 Pro Pro Glu Gly Trp Arg Ser Pro Arg Ser Gln Lys Thr Ala Ala 1695
 1685 1690 1695
 Gly Gly Gly Pro Gln Gly Lys Lys Gly Lys Asn Glu Pro Lys Val 1710
 1700 1705 1710
 Asp Ala Thr Arg Pro Glu Ala Thr Thr Glu Val Gly Pro Gln Ile 1725
 1715 1720 1725
 Gly Val Lys Glu Ser Ser Met Glu Pro Lys Ala Ala Glu Glu Glu 1740
 1730 1735 1740
 Ala Gly Ser Glu Gln Lys Arg Asp Arg Lys Asp Ala Gly Thr Asp 1755
 1745 1750 1755
 Lys Asn Pro Pro Glu Thr Ala Pro Val Glu Val Val Glu Lys Lys 1770
 1760 1765 1770
 Pro Ala Pro Glu Lys Asn Ser Lys Ser Lys Arg Gly Arg Ser Arg 1785
 1775 1780 1785
 Asn Ser Arg Leu Ala Val Asp Lys Ser Ala Ser Leu Lys Asn Val 1800
 1790 1795 1800
 Asp Ala Ala Val Ser Pro Arg Gly Ala Ala Ala Gln Ala Gly Glu 1815
 1805 1810 1815
 Arg Glu Ser Gly Val Val Ala Val Ser Pro Glu Lys Ser Glu Ser 1830
 1820 1825 1830
 Pro Gln Lys Glu Asp Gly Leu Ser Ser Gln Leu Lys Ser Asp Pro 1845
 1835 1840 1845
 Val Asp Pro Asp Lys Glu Pro Glu Lys Glu Asp Val Ser Ala Ser 1860
 1850 1855 1860

Gly Pro Ser Pro Glu Ala Thr Gln Leu Ala Lys Gln Met Glu Leu 1875
 1865
 Glu Gln Ala Val Glu His Ile Ala Lys Leu Ala Glu Ala Ser Ala 1880
 1885
 Ser Ala Ala Tyr Lys Ala Asp Ala Pro Glu Gly Leu Ala Pro Glu 1900
 1895
 Asp Arg Asp Lys Pro Ala His Gln Ala Ser Glu Thr Glu Leu Ala 1915
 1910
 Ala Ala Ile Gly Ser Ile Ile Asn Asp Ile Ser Gly Glu Pro Glu 1925
 1930
 Asn Phe Pro Ala Pro Pro Tyr Pro Gly Glu Ser Gln Thr Asp 1940
 1945
 Leu Gln Pro Pro Ala Gly Ala Gln Ala Leu Gln Pro Ser Glu Glu 1955
 1960
 Gly Met Glu Thr Asp Glu Ala Val Ser Gly Ile Leu Glu Thr Glu 1970
 1975
 Ala Ala Thr Glu Ser Ser Arg Pro Pro Val Asn Ala Pro Asp Pro 1985
 1990
 Ser Ala Gly Pro Thr Asp Thr Lys Glu Ala Arg Gly Asn Ser Ser 2000
 2005
 Glu Thr Ser His Ser Val Pro Glu Ala Lys Gly Ser Lys Glu Val 2015
 2020
 Glu Val Thr Leu Val Arg Lys Asp Lys Gly Arg Gln Lys Thr Thr 2030
 2035
 Arg Ser Arg Arg Lys Arg Asn Thr Asn Lys Lys Val Val Ala Pro 2045
 2050
 Val Glu Ser His Val Pro Glu Ser Asn Gln Ala Gln Gly Glu Ser 2060
 2065
 Pro Ala Ala Asn Glu Gly Thr Thr Val Gln His Pro Glu Ala Pro 2075
 2080
 Gln Glu Glu Lys Gln Ser Glu Lys Pro His Ser Thr Pro Pro Gln 2090
 2095
 Ser Cys Thr Ser Asp Leu Ser Lys Ile Pro Ser Thr Glu Asn Ser 2105
 2110
 Ser Gln Glu Ile Ser Val Glu Glu Arg Thr Pro Thr Lys Ala Ser 2120
 2125
 Val Pro Pro Asp Leu Pro Pro Pro Gln Pro Ala Pro Val Asp 2135
 2140
 Glu Glu Pro Gln Ala Arg Phe Arg Val His Ser Ile Ile Glu Ser 2150
 2155
 Asp Pro Val Thr Pro Pro Ser Asp Pro Ser Ile Pro Ile Pro Thr

2165 2170 2175
 Leu Pro Ser Val Thr Ala Ala Lys Leu Ser Pro Pro Val Ala Ser 2180
 2185
 Gly Gly Ile Pro His Gln Ser Pro Pro Thr Lys Val Thr Glu Trp 2195
 2200
 Ile Thr Arg Gln Glu Glu Pro Arg Ala Gln Ser Thr Pro Ser Pro 2210
 2215
 Ala Leu Pro Pro Asp Thr Lys Ala Ser Asp Val Asp Thr Ser Ser 2225
 2230
 Ser Thr Leu Arg Lys Ile Leu Met Asp Pro Lys Tyr Val Ser Ala 2240
 2245
 Thr Ser Val Thr Ser Thr Ser Val Thr Thr Ala Ile Ala Glu Pro 2255
 2260
 Val Ser Ala Ala Pro Cys Leu His Glu Ala Pro Pro Pro Val 2270
 2275
 Asp Ser Lys Lys Pro Leu Glu Lys Thr Ala Pro Pro Val Thr 2285
 2290
 Asn Asn Ser Glu Ile Gln Ala Ser Glu Val Leu Val Ala Ala Asp 2300
 2305
 Lys Glu Lys Val Ala Pro Val Ile Ala Pro Lys Ile Thr Ser Val 2315
 2320
 Ile Ser Arg Met Pro Val Ser Ile Asp Leu Glu Asn Ser Gln Lys 2330
 2335
 Ile Thr Leu Ala Lys Pro Ala Pro Gln Thr Leu Thr Gly Leu Val 2345
 2350
 Ser Ala Leu Thr Gly Leu Val Asn Val Ser Leu Val Pro Val Asn 2360
 2365
 Ala Leu Lys Gly Pro Val Lys Gly Ser Val Thr Thr Leu Lys Ser 2375
 2380
 Leu Val Ser Thr Pro Ala Gly Pro Val Asn Val Leu Lys Gly Pro 2390
 2395
 Val Asn Val Leu Thr Gly Pro Val Asn Val Leu Thr Thr Pro Val 2405
 2410
 Asn Ala Thr Val Gly Thr Val Asn Ala Ala Pro Gly Thr Val Asn 2420
 2425
 Ala Ala Ala Ser Ala Val Asn Ala Thr Ala Ser Ala Val Thr Val 2435
 2440
 Thr Ala Gly Ala Val Thr Ala Ala Ser Gly Gly Val Thr Ala Thr 2450
 2455
 Thr Gly Thr Val Thr Met Ala Gly Ala Val Ile Ala Pro Ser Thr 2465
 2470

Lys Cys Lys Gln Arg Ala Ser Ala Asn Glu Asn Ser Arg Phe His
 2480 2485
 Pro Gly Ser Met Pro Val Ile Asp Asp Arg Pro Ala Asp Ala Gly
 2495 2500
 Ser Gly Ala Gly Leu Arg Val Asn Thr Ser Glu Gly Val Val Leu
 2510 2515
 Leu Ser Tyr Ser Gly Gln Lys Thr Glu Gly Pro Gln Arg Ile Ser
 2525 2530
 Ala Lys Ile Ser Gln Ile Pro Pro Ala Ser Ala Met Asp Ile Glu
 2540 2545
 Phe Gln Gln Ser Val Ser Lys Ser Gln Val Lys Pro Asp Ser Val
 2555 2560
 Thr Ala Ser Gln Pro Pro Ser Lys Gly Pro Gln Ala Pro Ala Gly
 2570 2575
 Tyr Ala Asn Val Ala Thr His Ser Thr Leu Val Leu Thr Ala Gln
 2585 2590
 Thr Tyr Asn Ala Ser Pro Val Ile Ser Ser Val Lys Ala Asp Arg
 2600 2605
 Pro Ser Leu Glu Lys Pro Glu Pro Ile His Leu Ser Val Ser Thr
 2615 2620
 Pro Val Thr Gln Gly Gly Thr Val Lys Val Leu Thr Gln Gly Ile
 2630 2635
 Asn Thr Pro Pro Val Leu Val His Asn Gln Leu Val Leu Thr Pro
 2645 2650
 Ser Ile Val Thr Asn Lys Lys Leu Ala Asp Pro Val Thr Leu
 2660 2665
 Lys Ile Glu Thr Lys Val Leu Gln Pro Ala Asn Leu Gly Ser Thr
 2675 2680
 Leu Thr Pro His His Pro Pro Ala Leu Pro Ser Lys Leu Pro Thr
 2690 2695
 Glu Val Asn His Val Pro Ser Gly Pro Ser Ile Pro Ala Asp Arg
 2705 2710
 Thr Val Ser His Leu Ala Ala Ala Lys Leu Asp Ala His Ser Pro
 2720 2725
 Arg Pro Ser Gly Pro Gly Pro Ser Ser Phe Pro Arg Ala Ser His
 2735 2740
 Pro Ser Ser Thr Ala Ser Thr Ala Leu Ser Thr Asn Ala Thr Val
 2750 2755
 Met Leu Ala Ala Gly Ile Pro Val Pro Gln Phe Ile Ser Ser Ile
 2765 2770
 His Pro Glu Gln Ser Val Ile Met Pro Pro His Ser Ile Thr Gln
 2780 2785

Thr Val Ser Leu Ser His Leu Ser Gln Gly Glu Val Arg Met Asn
 2795 2800
 Thr Pro Thr Leu Pro Ser Ile Thr Tyr Ser Ile Arg Pro Glu Ala
 2810 2815
 Leu His Ser Pro Arg Ala Pro Leu Gln Pro Gln Gln Ile Glu Val
 2825 2830
 Arg Ala Pro Gln Arg Ala Ser Thr Pro Gln Pro Ala Pro Ala Gly
 2840 2845
 Val Pro Ala Leu Ala Ser Gln His Pro Pro Glu Glu Glu Val His
 2855 2860
 Tyr His Leu Pro Val Ala Arg Ala Thr Ala Pro Val Gln Ser Glu
 2870 2875
 Val Leu Val Met Gln Ser Glu Tyr Arg Leu His Pro Tyr Thr Val
 2885 2890
 Pro Arg Asp Val Arg Ile Met Val His Pro His Val Thr Ala Val
 2900 2905
 Ser Glu Gln Pro Arg Ala Ala Asp Gly Val Val Lys Val Pro Pro
 2915 2920
 Ala Ser Lys Ala Pro Gln Gln Pro Gly Lys Glu Ala Ala Lys Thr
 2930 2935
 Pro Asp Ala Lys Ala Ala Pro Thr Pro Thr Pro Ala Pro Val Pro
 2945 2950
 Val Pro Val Pro Leu Pro Ala Pro Ala Pro Ala Pro His Gly Glu
 2960 2965
 Ala Arg Ile Leu Thr Val Thr Pro Ser Asn Gln Leu Gln Gly Leu
 2975 2980
 Pro Leu Thr Pro Pro Val Val Thr His Gly Val Gln Ile Val
 2990 2995
 His Ser Ser Gly Glu Leu Phe Gln Glu Tyr Arg Tyr Gly Asp Ile
 3005 3010
 Arg Thr Tyr His Pro Pro Ala Gln Leu Thr His Thr Gln Phe Pro
 3020 3025
 Ala Ala Ser Ser Val Gly Leu Pro Ser Arg Thr Lys Thr Ala Ala
 3035 3040
 Gln Gly Pro Pro Pro Glu Gly Glu Pro Leu Gln Pro Pro Gln Pro
 3050 3055
 Val Gln Ser Thr Gln Pro Ala Gln Pro Ala Pro Pro Cys Pro Pro
 3065 3070
 Ser Gln Leu Gly Gln Pro Gly Gln Pro Pro Ser Ser Lys Met Pro
 3080 3085
 Gln Val Ser Gln Glu Ala Lys Gly Thr Gln Thr Gly Val Glu Gln

3095 3100 3105
 Pro Arg Leu Pro Ala Gly Pro Ala Asn Arg Pro Glu Pro His 3120
 3110 3115
 Thr Gln Val Gln Arg Ala Gln Ala Glu Thr Gly Pro Thr Ser Phe 3135
 3125 3130 3135
 Pro Ser Pro Val Ser Val Ser Met Lys Pro Asp Leu Pro Val Ser 3150
 3140 3145 3150
 Leu Pro Thr Gln Thr Ala Pro Lys Gln Pro Leu Phe Val Pro Thr 3165
 3155 3160 3165
 Thr Ser Gly Pro Ser Thr Pro Pro Gly Leu Val Leu Pro His Thr 3180
 3170 3175 3180
 Glu Phe Gln Pro Ala Pro Lys Gln Asp Ser Ser Pro His Leu Thr 3195
 3185 3190 3195
 Ser Gln Arg Pro Val Asp Met Val Gln Leu Leu Lys Lys Tyr Pro 3210
 3200 3205 3210
 Ile Val Trp Gln Gly Leu Leu Ala Leu Lys Asn Asp Thr Ala Ala 3225
 3215 3220 3225
 Val Gln Leu His Phe Val Ser Gly Asn Asn Val Leu Ala His Arg 3240
 3230 3235 3240
 Ser Leu Pro Leu Ser Glu Gly Gly Pro Pro Leu Arg Ile Ala Gln 3255
 3245 3250 3255
 Arg Met Arg Leu Glu Ala Thr Gln Leu Glu Gly Val Ala Arg Arg 3270
 3260 3265 3270
 Met Thr Val Glu Thr Asp Tyr Cys Leu Leu Leu Ala Leu Pro Cys 3285
 3275 3280 3285
 Gly Arg Asp Gln Glu Asp Val Val Ser Gln Thr Glu Ser Leu Lys 3300
 3290 3295 3300
 Ala Ala Phe Ile Thr Tyr Leu Gln Ala Lys Gln Ala Ala Gly Ile 3315
 3305 3310 3315
 Ile Asn Val Pro Asn Pro Gly Ser Asn Gln Pro Ala Tyr Val Leu 3330
 3320 3325 3330
 Gln Ile Phe Pro Pro Cys Glu Phe Ser Glu Ser His Leu Ser Arg 3345
 3335 3340 3345
 Leu Ala Pro Asp Leu Leu Ala Ser Ile Ser Asn Ile Ser Pro His 3360
 3350 3355 3360
 Leu Met Ile Val Ile Ala Ser Val 3370
 3365 3370
 <210> 172
 <211> 684
 <212> PRT
 <213> Homo sapiens
 <400> 172

350

Met Glu Asn Leu Gln Thr Asn Phe Ser Leu Val Gln Gly Ser Thr Lys 15
 1 5 10
 Lys Leu Asn Gly Met Gly Asp Asp Gly Ser Pro Pro Ala Lys Lys Met 30
 20 25 30
 Ile Thr Asp Ile His Val Asn Gly Lys Thr Ile Asn Lys Val Pro Thr 45
 35 40 45
 Val Lys Lys Glu His Leu Asp Asp Tyr Gly Glu Ala Pro Val Glu Thr 60
 50 55 60
 Asp Gly Glu His Val Lys Arg Thr Cys Thr Ser Val Pro Glu Thr Leu 80
 65 70 75
 His Leu Asn Pro Ser Leu Lys His Thr Leu Ala Gln Phe His Leu Ser 95
 85 90 95
 Ser Gln Ser Ser Leu Gly Gly Pro Ala Ala Phe Ser Ala Arg His Ser 110
 100 105 110
 Gln Glu Ser Met Ser Thr Thr Val Phe Leu Pro Leu Pro Ser Pro Gln 125
 115 120 125
 Val Leu Pro Gly Pro Leu Leu Ile Pro Ser Asp Ser Ser Thr Glu Leu 140
 130 135 140
 Thr Gln Thr Val Leu Glu Gly Glu Ser Ile Ser Cys Phe Gln Val Gly 160
 145 150 155
 Gly Glu Lys Arg Leu Cys Leu Pro Gln Val Leu Asn Ser Val Leu Arg 175
 165 170 175
 Glu Phe Thr Leu Gln Gln Ile Asn Thr Val Cys Asp Glu Leu Tyr Ile 190
 180 185 190
 Tyr Cys Ser Arg Cys Thr Ser Asp Gln Leu His Ile Leu Lys Val Leu 205
 195 200 205
 Gly Ile Leu Pro Phe Asn Ala Pro Ser Cys Gly Leu Ile Thr Leu Thr 220
 210 215 220
 Asp Ala Gln Arg Leu Cys Asn Ala Leu Leu Arg Pro Arg Thr Phe Pro 240
 225 230 235
 Gln Asn Gly Ser Val Leu Pro Ala Lys Ser Ser Leu Ala Gln Leu Lys 255
 245 250 255
 Glu Thr Gly Ser Ala Phe Glu Val Glu His Glu Cys Leu Gly Lys Cys 270
 260 265 270
 Gln Gly Leu Phe Ala Pro Gln Phe Tyr Val Gln Pro Asp Ala Pro Cys 285
 275 280 285
 Ile Gln Cys Leu Glu Cys Cys Gly Met Phe Ala Pro Gln Thr Phe Val 300
 290 295 300
 Met His Ser His Arg Ser Pro Asp Lys Arg Thr Cys His Trp Gly Phe 320
 305 310 315
 Glu Ser Ala Lys Trp His Cys Tyr Leu His Val Asn Gln Lys Tyr Leu 335
 325 330 335

351

Gly Thr Pro Glu Glu Lys Lys Leu Lys Ile Ile Leu Glu Glu Met Lys
340 345 350
Glu Lys Phe Ser Met Arg Ser Gly Lys Arg Asn Gln Ser Lys Thr Asp
355 360 365
Ala Pro Ser Gly Met Glu Glu Lys Ser Trp Tyr Pro Val Ile Lys Gln
370 375 380
Glu Gly Asp His Val Ser Gln Thr His Ser Phe Leu His Pro Ser Tyr
385 390 395 400
Tyr Leu Tyr Met Cys Asp Lys Val Val Ala Pro Asn Val Ser¹ Leu Thr
405 410 415
Ser Ala Val Ser Gln Ser Lys Glu Leu Thr Lys Thr Glu Ala Ser Lys
420 425 430
Ser Ile Ser Arg Gln Ser Glu Lys Ala His Ser Ser Gly Lys Leu Gln
435 440 445
Lys Thr Val Ser Tyr Pro Asp Val Ser Leu Glu Gln Glu Lys Met
450 455 460
Asp Leu Lys Thr Ser Arg Glu Leu Cys Ser Arg Leu Asp Ala Ser Ile
465 470 475 480
Ser Asn Asn Ser Thr Ser Lys Arg Lys Ser Glu Ser Ala Thr Cys Asn
485 490 495
Leu Val Arg Asp Ile Asn Lys Val Gly Ile Gly Leu Val Ala Ala
500 505 510
Ser Ser Pro Leu Leu Val Lys Asp Val Ile Cys Glu Asp Asp Lys Gly
515 520 525
Lys Ile Met Glu Glu Val Met Arg Thr Tyr Leu Lys Gln Gln Lys
530 535 540
Leu Asn Leu Ile Leu Gln Lys Lys Gln Gln Leu Leu Met Glu Val Lys
545 550 555 560
Met Leu Ser Ser Ser Lys Ser Met Lys Glu Leu Thr Glu Gln Gln
565 570 575
Asn Leu Gln Lys Glu Leu Ser Leu Gln Asn Glu His Ala Gln Arg
580 585 590
Met Glu Glu Phe Tyr Val Glu Gln Lys Asp Leu Glu Lys Leu Glu
595 600 605
Gln Ile Met Lys Gln Lys Cys Thr Cys Asp Ser Asn Leu Lys Asp
610 615 620
Lys Glu Ala Glu Tyr Ala Gly Gln Leu Ala Glu Leu Arg Gln Arg Leu
625 630 635 640
Asp His Ala Glu Ala Asp Arg Gln Glu Leu Gln Asp Glu Leu Arg Gln
645 650 655
Glu Arg Glu Ala Arg Gln Lys Leu Glu Met Ile Lys Glu Leu Lys

352

670

665

660

Leu Gln Ile Leu Lys Ser Ser Lys Thr Ala Lys Glu
675 680
<210> 173
<211> 550
<212> PRT
<213> Homo sapiens
<400> 173
Met Trp Lys Ala Ser Ala Gly His Ala Val Ser Ile Ala Gln Asp Asp
1 5 10 15
Ala Gly Ala Asp Asp Trp Glu Thr Asp Pro Asp Phe Val Asn Asp Val
20 25 30
Ser Glu Lys Glu Gln Arg Trp Gly Ala Lys Thr Val Gln Gly Ser Gly
35 40 45
His Gln Glu His Ile Asn Ile His Lys Leu Arg Glu Asn Val Phe Gln
50 55 60
Glu His Gln Thr Leu Lys Glu Lys Glu Leu Thr Gly Pro Lys Ala
65 70 75 80
Ser His Gly Tyr Gly Gly Lys Phe Gly Val Glu Gln Asp Arg Met Asp
85 90 95
Lys Ser Ala Val Gly His Glu Tyr Gln Ser Lys Leu Ser Lys His Cys
100 105 110
Ser Gln Val Asp Ser Val Arg Gly Phe Gly Lys Phe Gly Val Gln
115 120 125
Met Asp Arg Val Asp Gln Ser Ala Val Gly Phe Glu Tyr Gln Gly Lys
130 135 140
Thr Glu Lys His Ala Ser Gln Lys Asp Tyr Ser Ser Gly Phe Gly Gly
145 150 155 160
Lys Tyr Gly Val Gln Ala Asp Arg Val Asp Lys Ser Ala Val Gly Phe
165 170 175
Asp Tyr Gln Gly Lys Thr Glu Lys His Glu Ser Gln Arg Asp Tyr Ser
180 185 190
Lys Gly Phe Gly Gly Lys Tyr Gly Ile Asp Lys Asp Lys Val Asp Lys
195 200 205
Ser Ala Val Gly Phe Glu Tyr Gln Gly Lys Thr Glu Lys His Glu Ser
210 215 220
Gln Lys Asp Tyr Val Lys Gly Phe Gly Gly Lys Phe Gly Val Gln Thr
225 230 235 240
Asp Arg Gln Asp Lys Cys Ala Leu Gly Trp Asp His Gln Glu Lys Leu
245 250 255
Gln Leu His Glu Ser Gln Lys Asp Tyr Lys Thr Gly Phe Gly Gly Lys
260 265 270

353

Phe Gly Val Gln Ser Glu Arg Gln Asp Ser Ala Ala Val Gly Phe Asp 275 280
 Tyr Lys Glu Lys Leu Ala Lys His Glu Ser Gln Gln Asp Tyr Ser Lys 290 300
 Gly Phe Gly Gly Lys Tyr Gly Val Gln Lys Asp Arg Met Asp Lys Asn 305 310 315 320
 Ala Ser Thr Phe Glu Asp Val Thr Gln Val Ser Ser Ala Tyr Gln Lys 325 330 335
 Thr Val Pro Val Glu Ala Val Thr Ser Lys Thr Ser Asn Ile Arg Ala 340 345 350
 Asn Phe Glu Asn Leu Ala Lys Glu Lys Glu Gln Asp Arg Arg Lys 355 360 365
 Ala Glu Ala Glu Arg Ala Gln Arg Met Ala Lys Glu Arg Gln Gln 370 375 380
 Glu Glu Ala Arg Arg Lys Leu Glu Gln Ala Arg Ala Lys Thr Gln 385 390 395 400
 Thr Pro Pro Val Ser Pro Ala Pro Gln Pro Thr Glu Glu Arg Leu Pro 405 410 415
 Ser Ser Pro Val Tyr Glu Asp Ala Ala Ser Phe Lys Ala Glu Leu Ser 420 425 430
 Tyr Arg Gly Pro Val Ser Gly Thr Glu Pro Glu Pro Val Tyr Ser Met 435 440 445
 Glu Ala Ala Asp Tyr Arg Glu Ala Ser Ser Gln Gln Gly Leu Ala Tyr 450 455 460
 Ala Thr Glu Ala Val Tyr Glu Ser Ala Glu Ala Pro Gly His Tyr Pro 465 470 475 480
 Ala Glu Asp Ser Thr Tyr Asp Glu Tyr Glu Asn Asp Leu Gly Tyr Thr 485 490 495
 Ala Val Ala Leu Tyr Asp Tyr Gln Ala Ala Gly Asp Asp Glu Ile Ser 500 505 510
 Phe Asp Pro Asp Asp Ile Ile Thr Asn Ile Glu Met Ile Asp Asp Gly 515 520 525
 Trp Trp Arg Gly Val Cys Lys Gly Arg Tyr Gly Leu Phe Pro Ala Asn 530 535 540
 Tyr Val Glu Leu Arg Gln 545 550
 <210> 174
 <211> 486
 <212> PRT
 <213> Homo sapiens
 <400> 174
 Met Trp Lys Ser Val Val Gly His Asp Val Ser Val Ser Val Glu Thr 1 5 10 15
 354

Gln Gly Asp Asp Trp Asp Thr Asp Pro Asp Phe Val Asn Asp Ile Ser 20 25 30
 Glu Lys Glu Gln Arg Trp Gly Ala Lys Thr Ile Glu Gly Ser Gly Arg 35 40 45
 Thr Glu His Ile Asn Ile His Gln Leu Arg Asn Lys Val Ser Glu Glu 50 55 60
 His Asp Val Leu Arg Lys Lys Glu Met Glu Ser Gly Pro Lys Ala Ser 65 70 75 80
 His Gly Tyr Gly Gly Arg Phe Gly Val Glu Arg Asp Arg Met Asp Lys 85 90 95
 Ser Ala Val Gly His Glu Tyr Val Ala Glu Val Glu Lys His Ser Ser 100 105 110
 Gln Thr Asp Ala Ala Lys Gly Phe Gly Gly Lys Tyr Gly Val Glu Arg 115 120 125
 Asp Arg Ala Asp Lys Ser Ala Val Gly Phe Asp Tyr Lys Gly Glu Val 130 135 140
 Glu Lys His Thr Ser Gln Lys Asp Tyr Ser Arg Gly Phe Gly Gly Arg 145 150 155 160
 Tyr Gly Val Glu Lys Asp Lys Trp Asp Lys Ala Ala Leu Gly Tyr Asp 165 170 175
 Tyr Lys Gly Glu Thr Glu Lys His Glu Ser Gln Arg Asp Tyr Ala Lys 180 185 190
 Gly Phe Gly Gly Gln Tyr Gly Ile Gln Lys Asp Arg Val Asp Lys Ser 195 200 205
 Ala Val Gly Phe Asn Glu Met Glu Ala Pro Thr Thr Ala Tyr Lys Lys 210 215 220
 Thr Thr Pro Ile Glu Ala Ala Ser Ser Gly Ala Arg Gly Leu Lys Ala 225 230 235 240
 Lys Phe Glu Ser Met Ala Glu Glu Lys Arg Lys Arg Glu Glu Glu 245 250 255
 Lys Ala Gln Gln Val Ala Arg Arg Gln Gln Glu Arg Lys Ala Val Thr 260 265 270
 Lys Arg Ser Pro Glu Ala Pro Gln Pro Val Ile Ala Met Glu Glu Pro 275 280 285
 Ala Val Pro Ala Pro Leu Pro Lys Lys Ile Ser Ser Glu Ala Trp Pro 290 295 300
 Pro Val Gly Thr Pro Pro Ser Ser Glu Ser Glu Pro Val Arg Thr Ser 305 310 315 320
 Arg Glu His Pro Val Pro Leu Leu Pro Ile Arg Gln Thr Leu Pro Glu 325 330 335
 Asp Asn Glu Glu Pro Pro Ala Leu Pro Pro Arg Thr Leu Glu Gly Leu 340 345 350
 355

340 345 350
 Gln Val Glu Glu Pro Val Tyr Glu Ala Glu Pro Glu Pro Glu Pro
 355 360 365
 Glu Pro Glu Pro Glu Pro Glu Asn Asp Tyr Glu Asp Val Glu Glu Met
 370 375 380
 Asp Arg His Glu Glu Asp Glu Pro Glu Glu Asp Tyr Glu Glu Val
 385 390 395 400
 Leu Glu Pro Glu Asp Ser Ser Phe Ser Ser Ala Leu Ala Gly Ser Ser
 405 410 415
 Gly Cys Pro Ala Gly Ala Gly Ala Val Ala Leu Gly Ile Ser
 420 425 430
 Ala Val Ala Leu Tyr Asp Tyr Glu Glu Gly Ser Asp Glu Leu Ser
 435 440 445
 Phe Asp Pro Asp Asp Val Ile Thr Asp Ile Glu Met Val Asp Glu Gly
 450 455 460
 Trp Trp Arg Gly Arg Cys His Gly His Phe Gly Leu Phe Pro Ala Asn
 465 470 475 480
 Tyr Val Lys Leu Leu Glu
 485
 <210> 175
 <211> 466
 <212> PRT
 <213> Homo sapiens
 <400> 175
 Met Ser Tyr Pro Gly Tyr Pro Pro Thr Gly Tyr Pro Pro Phe Pro Gly
 1 5 10 15
 Tyr Pro Pro Ala Gly Gln Glu Ser Ser Phe Pro Pro Ser Gly Gln Tyr
 20 25 30
 Pro Tyr Pro Ser Gly Phe Pro Pro Met Gly Gly Ala Tyr Pro Gln
 35 40 45
 Val Pro Ser Ser Gly Tyr Pro Gly Ala Gly Tyr Pro Ala Pro Gly
 50 55 60
 Gly Tyr Pro Ala Pro Gly Gly Tyr Pro Gly Ala Pro Gln Pro Gly Gly
 65 70 75 80
 Ala Pro Ser Tyr Pro Gly Val Pro Pro Gly Gln Gly Phe Gly Val Pro
 85 90 95
 Pro Gly Gly Ala Gly Phe Ser Gly Tyr Pro Gln Pro Pro Ser Gln Ser
 100 105 110
 Tyr Gly Gly Gly Pro Ala Gln Val Pro Leu Pro Gly Gly Phe Pro Gly
 115 120 125
 Gly Gln Met Pro Ser Gln Tyr Pro Gly Gln Pro Thr Tyr Pro Ser
 130 135 140

356

Gln Pro Ala Thr Val Thr Gln Val Thr Gln Gly Thr Ile Arg Pro Ala
 145 150 155 160
 Ala Asn Phe Asp Ala Ile Arg Asp Ala Glu Ile Leu Arg Lys Ala Met
 165 170 175
 Lys Gly Phe Gly Thr Asp Glu Gln Ala Ile Val Asp Val Val Ala Asn
 180 185 190
 Arg Ser Asn Asp Gln Arg Gln Lys Ile Lys Ala Ala Phe Lys Thr Ser
 195 200 205
 Tyr Gly Lys Asp Leu Ile Lys Asp Leu Lys Ser Glu Leu Ser Gly Asn
 210 215 220
 Met Glu Glu Leu Ile Leu Ala Leu Phe Met Pro Pro Thr Tyr Tyr Asp
 225 230 235 240
 Ala Trp Ser Leu Arg Lys Ala Met Gln Gly Ala Gly Thr Gln Glu Arg
 245 250 255
 Val Leu Ile Glu Ile Leu Cys Thr Arg Thr Asn Gln Glu Ile Arg Glu
 260 265 270
 Ile Val Arg Cys Tyr Gln Ser Glu Phe Gly Arg Asp Leu Glu Lys Asp
 275 280 285
 Ile Arg Ser Asp Thr Ser Gly His Phe Glu Arg Leu Leu Val Ser Met
 290 295 300
 Cys Gln Gly Asn Arg Asp Glu Asn Gln Ser Ile Asn His Gln Met Ala
 305 310 315 320
 Gln Glu Asp Ala Gln Arg Leu Tyr Gln Ala Gly Glu Gly Arg Leu Gly
 325 330 335
 Thr Asp Glu Ser Cys Phe Asn Met Ile Leu Ala Thr Arg Ser Phe Pro
 340 345 350
 Gln Leu Arg Ala Thr Met Glu Ala Tyr Ser Arg Met Ala Asn Arg Asp
 355 360 365
 Leu Leu Ser Ser Val Ser Arg Glu Phe Ser Gly Tyr Val Glu Ser Gly
 370 375 380
 Leu Lys Thr Ile Leu Gln Cys Ala Leu Asn Arg Pro Ala Phe Phe Ala
 385 390 395 400
 Glu Arg Leu Tyr Tyr Ala Met Lys Gly Ala Gly Thr Asp Asp Ser Thr
 405 410 415
 Leu Val Arg Ile Val Val Thr Arg Ser Glu Ile Asp Leu Val Gln Ile
 420 425 430
 Lys Gln Met Phe Ala Gln Met Tyr Gln Lys Thr Leu Gly Thr Met Ile
 435 440 445
 Ala Gly Asp Thr Ser Gly Asp Tyr Arg Arg Leu Leu Ala Ile Val
 450 455 460
 Gly Gln
 465

357

<210> 176
 <211> 505
 <212> PRT
 <213> Homo sapiens
 <400> 176
 Met Ser Tyr Pro Gly Tyr Pro Pro Pro Gly Tyr Tyr Pro Pro Ala
 1 5 10 15
 Ala Pro Gly Gly Gly Pro Tyr Gly Gly Ala Ala Tyr Pro Pro Pro
 20 25 30
 Ser Met Pro Pro Ile Gly Leu Asp Asn Val Ala Thr Tyr Ala Gly Gln
 35 40 45
 Phe Asn Gln Asp Tyr Leu Ser Gly Met Ala Ala Asn Met Ser Gly Thr
 50 55 60
 Phe Gly Gly Ala Asn Met Pro Asn Leu Tyr Pro Gly Ala Pro Gly Ala
 65 70 75 80
 Gly Tyr Pro Pro Val Pro Gly Gly Phe Gly Gln Pro Pro Ser Ala
 85 90 95
 Gln Gln Pro Val Pro Tyr Gly Met Tyr Pro Pro Gly Gly Asn
 100 105 110
 Pro Pro Ser Arg Met Pro Ser Tyr Pro Tyr Pro Gly Ala Pro Val
 115 120 125
 Pro Gly Gln Pro Met Pro Pro Gly Gln Gln Pro Pro Gly Ala Tyr
 130 135 140
 Pro Gly Gln Pro Val Thr Tyr Pro Gly Gln Pro Pro Val Pro Leu
 145 150 155 160
 Pro Gly Gln Gln Pro Val Pro Ser Tyr Tyr Pro Gly Tyr Pro Gly Ser
 165 170 175
 Gly Thr Val Thr Pro Ala Val Pro Pro Thr Gln Phe Gly Ser Arg Gly
 180 185 190
 Thr Ile Thr Asp Ala Pro Gly Phe Asp Pro Leu Arg Asp Ala Glu Val
 195 200 205
 Leu Arg Lys Ala Met Lys Gly Phe Gly Thr Asp Gly Gln Ala Ile Ile
 210 215 220
 Asp Cys Leu Gly Ser Arg Ser Asn Lys Gln Arg Gln Gln Ile Leu Leu
 225 230 235 240
 Ser Phe Lys Thr Ala Tyr Gly Lys Asp Leu Ile Lys Asp Leu Lys Ser
 245 250 255
 Glu Leu Ser Gly Asn Phe Glu Lys Thr Ile Leu Ala Leu Met Lys Thr
 260 265 270
 Pro Val Leu Phe Asp Ile Tyr Glu Ile Lys Glu Ala Ile Lys Gly Val
 275 280 285
 Gly Thr Asp Glu Ala Cys Leu Ile Glu Ile Leu Ala Ser Arg Ser Asn
 290 295 300
 Glu His Ile Arg Glu Leu Asn Arg Ala Tyr Lys Ala Glu Phe Lys Lys
 305 310 315 320
 Thr Leu Glu Glu Ala Ile Arg Ser Asp Thr Ser Gly His Phe Gln Arg
 325 330 335
 Leu Leu Ile Ser Leu Ser Gln Gly Asn Arg Asp Glu Ser Thr Asn Val
 340 345 350
 Asp Met Ser Leu Ala Gln Arg Asp Ala Gln Glu Leu Tyr Ala Ala Gly
 355 360 365
 Glu Asn Arg Leu Gly Thr Asp Glu Ser Lys Phe Asn Ala Val Leu Cys
 370 375 380
 Ser Arg Ser Arg Ala His Leu Val Ala Val Phe Asn Glu Tyr Gln Arg
 385 390 395 400
 Met Thr Gly Arg Asp Ile Glu Lys Ser Ile Cys Arg Glu Met Ser Gly
 405 410 415
 Asp Leu Glu Glu Gly Met Leu Ala Val Lys Cys Leu Lys Asn Thr
 420 425 430
 Pro Ala Phe Phe Ala Glu Arg Leu Asn Lys Ala Met Arg Gly Ala Gly
 435 440 445
 Thr Lys Asp Arg Thr Leu Ile Arg Ile Met Val Ser Arg Ser Glu Thr
 450 455 460
 Asp Leu Leu Asp Ile Arg Ser Glu Tyr Lys Arg Met Tyr Gly Lys Ser
 465 470 475 480
 Leu Tyr His Asp Ile Ser Gly Asp Thr Ser Gly Asp Tyr Arg Lys Ile
 485 490 495
 Leu Leu Lys Ile Cys Gly Gly Asn Asp
 500 505
 <210> 177
 <211> 515
 <212> PRT
 <213> Homo sapiens
 <400> 177
 Met Glu Ala Arg Glu Pro Gly Arg Pro Thr Thr Tyr His Leu Val
 1 5 10 15
 Pro Asn Thr Ser Gln Ser Gln Val Glu Glu Asp Val Ser Ser Pro Pro
 20 25 30
 Gln Arg Ser Ser Glu Thr Met Gln Leu Lys Lys Glu Ile Ser Leu Leu
 35 40 45
 Asn Gly Val Ser Leu Val Val Gly Asn Met Ile Gly Ser Gly Ile Phe
 50 55 60
 Val Ser Pro Lys Gly Val Leu Val His Thr Ala Ser Tyr Gly Met Ser
 65 70 75 80
 359

Leu Ile Val Trp Ala Ile Gly Gly Leu Phe Ser Val Val Gly Ala Leu 95
 Cys Tyr Ala Gly Leu Gly Thr Thr Ile Thr Lys Ser Gly Ala Ser Tyr 110
 Ala Tyr Ile Leu Glu Ala Phe Gly Gly Phe Ile Ala Phe Ile Arg Leu 125
 Trp Val Ser Leu Leu Val Val Glu Pro Thr Gly Gln Ala Ile Ile Ala 140
 Ile Thr Phe Ala Asn Tyr Ile Ile Gln Pro Ser Phe Pro Ser Cys Asp 160
 Pro Pro Tyr Leu Ala Cys Arg Leu Leu Ala Ala Cys Ile Cys Leu 175
 Leu Thr Phe Val Asn Cys Ala Tyr Val Lys Trp Gly Thr Arg Val Gln 190
 Asp Thr Phe Thr Tyr Ala Lys Val Val Ala Leu Ile Ala Ile Ile Val 205
 Met Gly Leu Val Lys Leu Cys Gln Gly His Ser Glu His Phe Gln Asp 220
 Ala Phe Glu Gly Ser Ser Trp Asp Met Gly Asn Leu Ser Leu Ala Leu 240
 Tyr Ser Ala Leu Phe Ser Tyr Ser Gly Trp Asp Thr Leu Asn Phe Val 255
 Thr Glu Glu Ile Lys Asn Pro Glu Arg Asn Leu Pro Leu Ala Ile Gly 270
 Ile Ser Met Pro Ile Val Thr Leu Ile Tyr Ile Leu Thr Asn Val Ala 285
 Tyr Tyr Thr Val Leu Asn Ile Ser Asp Val Leu Ser Ser Asp Ala Val 300
 Ala Val Thr Phe Ala Asp Gln Thr Phe Gly Met Phe Ser Trp Thr Ile 320
 Pro Ile Ala Val Ala Leu Ser Cys Phe Gly Gly Leu Asn Ala Ser Ile 335
 Phe Ala Ser Ser Arg Leu Phe Phe Val Gly Ser Arg Glu Gly His Leu 350
 Pro Asp Leu Leu Ser Met Ile His Ile Glu Arg Phe Thr Pro Ile Pro 365
 Ala Leu Leu Phe Asn Cys Thr Met Ala Leu Ile Tyr Leu Ile Val Glu 380
 Asp Val Phe Gln Leu Ile Asn Tyr Phe Ser Phe Ser Tyr Trp Phe Phe 400
 Val Gly Leu Ser Val Val Gly Gln Leu Tyr Leu Arg Trp Lys Glu Pro 415

360

Lys Arg Pro Arg Pro Leu Lys Leu Ser Val Phe Phe Pro Ile Val Phe 420
 Cys Ile Cys Ser Val Phe Leu Val Ile Val Pro Leu Phe Thr Asp Thr 445
 Ile Asn Ser Leu Ile Gly Ile Gly Ile Ala Leu Ser Gly Val Pro Phe 460
 Tyr Phe Met Gly Val Tyr Leu Pro Glu Ser Arg Arg Pro Leu Phe Ile 480
 Arg Asn Val Leu Ala Ala Ile Thr Arg Gly Thr Gln Gln Leu Cys Phe 495
 Cys Val Leu Thr Glu Leu Asp Val Ala Glu Glu Lys Lys Asp Glu Arg 510
 Lys Thr Asp 515
 <210> 178
 <211> 334
 <212> PRT
 <213> Homo sapiens
 <400> 178
 Met Ser Lys Leu Leu Asn Pro Glu Glu Met Thr Ser Arg Asp Tyr Tyr 15
 Phe Asp Ser Tyr Ala His Phe Gly Ile His Glu Glu Met Leu Lys Asp 30
 Glu Val Arg Thr Leu Thr Tyr Arg Asn Ser Met Tyr His Asn Lys His 45
 Val Phe Lys Asp Lys Val Val Leu Asp Val Gly Ser Gly Thr Gly Ile 60
 Leu Ser Met Phe Ala Ala Lys Ala Gly Ala Lys Lys Val Phe Gly Ile 80
 Glu Cys Ser Ser Ile Ser Asp Tyr Ser Glu Lys Ile Ile Lys Ala Asn 95
 His Leu Asp Asn Ile Ile Thr Ile Phe Lys Gly Lys Val Glu Glu Val 110
 Glu Leu Pro Val Glu Lys Val Asp Ile Ile Ile Ser Glu Trp Met Gly 125
 Tyr Cys Leu Phe Tyr Glu Ser Met Leu Asn Thr Val Ile Phe Ala Arg 140
 Asp Lys Trp Leu Lys Pro Gly Gly Leu Met Phe Pro Asp Arg Ala Ala 160
 Leu Tyr Val Val Ala Ile Glu Asp Arg Gln Tyr Lys Asp Phe Lys Ile 175
 His Trp Trp Glu Asn Val Tyr Gly Phe Asp Met Thr Cys Ile Arg Asp

361

180 185 190
 Val Ala Met Lys Glu Pro Leu Val Asp Ile Val Asp Pro Lys Glu Val
 195 200 205
 Val Thr Asn Ala Cys Leu Ile Lys Glu Val Asp Ile Tyr Thr Val Lys
 210 215 220
 Thr Glu Glu Leu Ser Phe Thr Ser Ala Phe Cys Leu Glu Ile Glu Arg
 225 230 235 240
 Asn Asp Tyr Val His Ala Leu Val Thr Tyr Phe Asn Ile Glu Phe Thr
 245 250 255
 Lys Cys His Lys Lys Met Gly Phe Ser Thr Ala Pro Asp Ala Pro Tyr
 260 265 270
 Thr His Trp Lys Glu Thr Val Phe Tyr Leu Glu Asp Tyr Leu Thr Val
 275 280 285
 Arg Arg Gly Glu Glu Ile Tyr Gly Thr Ile Ser Met Lys Pro Asn Ala
 290 295 300
 Lys Asn Val Arg Asp Leu Asp Phe Thr Val Asp Leu Asp Phe Lys Gly
 305 310 315 320
 Glu Leu Cys Glu Thr Ser Val Ser Asn Asp Tyr Lys Met Arg
 325 330
 <210> 179
 <211> 347
 <212> PRT
 <213> Homo sapiens
 <400> 179
 Met Val Gly Val Ala Glu Val Ser Cys Gly Glu Ala Glu Ser Ser Glu
 1 5 10 15
 Lys Pro Asn Ala Glu Asp Met Thr Ser Lys Asp Tyr Tyr Phe Asp Ser
 20 25 30
 Tyr Ala His Phe Gly Ile His Glu Glu Met Leu Lys Asp Glu Val Arg
 35 40 45
 Thr Leu Thr Tyr Arg Asn Ser Met Phe His Asn Arg His Leu Phe Lys
 50 55 60
 Asp Lys Val Val Leu Asp Val Gly Ser Gly Thr Gly Ile Leu Cys Met
 65 70 75 80
 Phe Ala Ala Lys Ala Gly Ala Arg Lys Val Ile Gly Ile Glu Cys Ser
 85 90 95
 Ser Ile Ser Asp Tyr Ala Val Lys Ile Val Lys Ala Asn Lys Leu Asp
 100 105 110
 His Val Val Thr Ile Ile Lys Gly Lys Val Glu Glu Val Glu Leu Pro
 115 120 125
 Val Glu Lys Val Asp Ile Ile Ser Glu Trp Met Gly Tyr Cys Leu
 130 135 140

Phe Tyr Glu Ser Met Leu Asn Thr Val Leu Tyr Ala Arg Asp Lys Trp
 145 150 155 160
 Leu Ala Pro Asp Gly Leu Ile Phe Pro Asp Arg Ala Thr Leu Tyr Val
 165 170 175
 Thr Ala Ile Glu Asp Arg Glu Tyr Lys Asp Tyr Lys Ile His Trp Trp
 180 185 190
 Glu Asn Val Tyr Gly Phe Asp Met Ser Cys Ile Lys Asp Val Ala Ile
 195 200 205
 Lys Glu Pro Leu Val Asp Val Val Asp Pro Lys Glu Leu Val Thr Asn
 210 215 220
 Ala Cys Leu Ile Lys Glu Val Asp Ile Tyr Thr Val Lys Val Glu Asp
 225 230 235 240
 Leu Thr Phe Thr Ser Pro Phe Cys Leu Glu Val Lys Arg Asn Asp Tyr
 245 250 255
 Val His Ala Leu Val Ala Tyr Phe Asn Ile Glu Phe Thr Arg Cys His
 260 265 270
 Lys Arg Thr Gly Phe Ser Thr Ser Pro Glu Ser Pro Tyr Thr His Trp
 275 280 285
 Lys Glu Thr Val Phe Tyr Met Glu Asp Tyr Leu Thr Val Lys Thr Gly
 290 295 300
 Glu Glu Ile Phe Gly Thr Ile Gly Met Arg Pro Asn Ala Lys Asn Asn
 305 310 315 320
 Arg Asp Leu Asp Phe Thr Ile Asp Leu Asp Phe Lys Gly Glu Leu Cys
 325 330 335
 Glu Leu Ser Cys Ser Thr Asp Tyr Arg Met Arg
 340 345
 <210> 180
 <211> 502
 <212> PRT
 <213> Homo sapiens
 <400> 180
 Met Leu Leu Arg Ser Ala Gly Lys Leu Asn Val Gly Thr Lys Lys Glu
 1 5 10 15
 Asp Gly Glu Ser Thr Ala Pro Thr Pro Arg Pro Lys Val Leu Arg Cys
 20 25 30
 Lys Cys His His Cys Pro Glu Asp Ser Val Asn Asn Ile Cys Ser
 35 40 45
 Thr Asp Gly Tyr Cys Phe Thr Met Ile Glu Glu Asp Asp Ser Gly Leu
 50 55 60
 Pro Val Val Thr Ser Gly Cys Leu Gly Leu Glu Gly Ser Asp Phe Glu
 65 70 75 80
 Cys Arg Asp Thr Pro Ile Pro His Glu Arg Arg Ser Ile Glu Cys Cys
 85 90 95

Thr Glu Arg Asn Glu Cys Asn Lys Asp Leu His Pro Thr Leu Pro Pro
 100 105 110
 Leu Lys Asn Arg Asp Phe Val Asp Gly Pro Ile His His Arg Ala Leu
 115 120 125
 Leu Ile Ser Val Thr Val Cys Ser Leu Leu Val Leu Ile Ile Leu
 130 135 140
 Phe Cys Tyr Phe Arg Tyr Lys Arg Gln Glu Thr Arg Pro Arg Tyr Ser
 145 150 155 160
 Ile Gly Leu Glu Gln Asp Glu Thr Tyr Ile Pro Pro Gly Glu Ser Leu
 165 170 175
 Arg Asp Leu Ile Glu Gln Ser Gln Ser Ser Gly Ser Gly Leu
 180 185 190
 Pro Leu Leu Val Gln Arg Thr Ile Ala Lys Gln Ile Gln Met Val Lys
 195 200 205
 Gln Ile Gly Lys Gly Arg Tyr Gly Glu Val Trp Met Gly Lys Trp Arg
 210 215 220
 Gly Glu Lys Val Ala Val Lys Val Phe Phe Thr Thr Glu Glu Ala Ser
 225 230 235 240
 Trp Phe Arg Glu Thr Glu Ile Tyr Gln Thr Val Leu Met Arg His Glu
 245 250 255
 Asn Ile Leu Gly Phe Ile Ala Ala Asp Ile Lys Gly Thr Gly Ser Trp
 260 265 270
 Thr Gln Leu Tyr Leu Ile Thr Asp Tyr His Glu Asn Gly Ser Leu Tyr
 275 280 285
 Asp Tyr Leu Lys Ser Thr Thr Leu Asp Ala Lys Ser Met Leu Lys Leu
 290 295 300
 Ala Tyr Ser Ser Val Ser Gly Leu Cys His Leu His Thr Glu Ile Phe
 305 310 315 320
 Ser Thr Gln Gly Lys Pro Ala Ile Ala His Arg Asp Leu Lys Ser Lys
 325 330 335
 Asn Ile Leu Val Lys Lys Asn Gly Thr Cys Cys Ile Ala Asp Leu Gly
 340 345 350
 Leu Ala Val Lys Phe Ile Ser Asp Thr Asn Glu Val Asp Ile Pro Pro
 355 360 365
 Asn Thr Arg Val Gly Thr Lys Arg Tyr Met Pro Pro Glu Val Leu Asp
 370 375 380
 Glu Ser Leu Asn Arg Asn His Phe Gln Ser Tyr Ile Met Ala Asp Met
 385 390 395 400
 Tyr Ser Phe Gly Leu Ile Leu Trp Glu Val Ala Arg Arg Cys Val Ser
 405 410 415
 Gly Gly Ile Val Glu Glu Tyr Gln Leu Pro Tyr His Asp Leu Val Pro

420 425 430
 Ser Asp Pro Ser Tyr Glu Asp Met Arg Glu Ile Val Cys Ile Lys Lys
 435 440 445
 Leu Arg Pro Ser Phe Pro Asn Arg Trp Ser Ser Asp Glu Cys Leu Arg
 450 455 460
 Gln Met Gly Lys Leu Met Thr Glu Cys Trp Ala His Asn Pro Ala Ser
 465 470 475 480
 Arg Leu Thr Ala Leu Arg Val Lys Lys Thr Leu Ala Lys Met Ser Glu
 485 490 495
 Ser Gln Asp Ile Lys Leu
 500
 <210> 181
 <211> 532
 <212> PRT
 <213> Homo sapiens
 <400> 181
 Met Thr Gln Leu Tyr Ile Tyr Ile Arg Leu Leu Gly Ala Tyr Leu Phe
 1 5 10 15
 Ile Ile Ser Arg Val Gln Gly Gln Asn Leu Asp Ser Met Leu His Gly
 20 25 30
 Thr Gly Met Lys Ser Asp Ser Asp Gln Lys Lys Ser Glu Asn Gly Val
 35 40 45
 Thr Leu Ala Pro Glu Asp Thr Leu Pro Phe Leu Lys Cys Tyr Cys Ser
 50 55 60
 Gly His Cys Pro Asp Asp Ala Ile Asn Asn Thr Cys Ile Thr Asn Gly
 65 70 75 80
 His Cys Phe Ala Ile Ile Glu Glu Asp Asp Gln Gly Glu Thr Thr Leu
 85 90 95
 Ala Ser Gly Cys Met Lys Tyr Glu Gly Ser Asp Phe Gln Cys Lys Asp
 100 105 110
 Ser Pro Lys Ala Gln Leu Arg Arg Thr Ile Glu Cys Cys Arg Thr Asn
 115 120 125
 Leu Cys Asn Gln Tyr Leu Gln Pro Thr Leu Pro Val Val Ile Gly
 130 135 140
 Pro Phe Phe Asp Gly Ser Ile Arg Trp Leu Val Leu Leu Ile Ser Met
 145 150 155 160
 Ala Val Cys Ile Ile Ala Met Ile Ile Phe Ser Ser Cys Phe Cys Tyr
 165 170 175
 Lys His Tyr Cys Lys Ser Ile Ser Ser Arg Arg Arg Tyr Asn Arg Asp
 180 185 190
 Leu Glu Gln Asp Glu Ala Phe Ile Pro Val Gly Glu Ser Leu Lys Asp
 195 200 205

Leu Ile Asp Gln Ser Gln Ser Gly Ser Gly Ser Gly Leu Pro Leu
 210 215 220
 Leu Val Gln Arg Thr Ile Ala Lys Gln Ile Gln Met Val Arg Gln Val
 225 230 235 240
 Gly Lys Gly Arg Tyr Gly Gln Val Trp Met Gly Lys Trp Arg Gly Gln
 245 250 255
 Lys Val Ala Val Lys Val Phe Thr Thr Gln Glu Ala Ser Trp Phe
 260 265 270
 Arg Glu Thr Glu Ile Tyr Gln Thr Val Leu Met Arg His Glu Asn Ile
 275 280 285
 Leu Gly Phe Ile Ala Ala Asp Ile Lys Gly Thr Gly Ser Trp Thr Gln
 290 295 300
 Leu Tyr Leu Ile Thr Asp Tyr His Glu Asn Gly Ser Leu Tyr Asp Phe
 305 310 315 320
 Leu Lys Cys Ala Thr Leu Asp Thr Arg Ala Leu Leu Lys Leu Ala Tyr
 325 330 335
 Ser Ala Ala Cys Gly Leu Cys His Leu His Thr Glu Ile Tyr Gly Thr
 340 345 350
 Gln Gly Lys Pro Ala Ile Ala His Arg Asp Leu Lys Ser Lys Asn Ile
 355 360 365
 Leu Ile Lys Lys Asn Gly Ser Cys Cys Ile Ala Asp Leu Gly Leu Ala
 370 375 380
 Val Lys Phe Asn Ser Asp Thr Asn Glu Val Asp Val Pro Leu Asn Thr
 385 390 395 400
 Arg Val Gly Thr Lys Arg Tyr Met Ala Pro Glu Val Leu Asp Glu Ser
 405 410 415
 Leu Asn Lys Asn His Phe Gln Pro Tyr Ile Met Ala Asp Ile Tyr Ser
 420 425 430
 Phe Gly Leu Ile Ile Trp Glu Met Ala Arg Arg Cys Ile Thr Gly Gly
 435 440 445
 Ile Val Glu Glu Tyr Gln Leu Pro Tyr Tyr Asn Met Val Pro Ser Asp
 450 455 460
 Pro Ser Tyr Glu Asp Met Arg Glu Val Val Cys Val Lys Arg Leu Arg
 465 470 475 480
 Pro Ile Val Ser Asn Arg Trp Asn Ser Asp Glu Cys Leu Arg Ala Val
 485 490 495
 Leu Lys Leu Met Ser Glu Cys Trp Ala His Asn Pro Ala Ser Arg Leu
 500 505 510
 Thr Ala Leu Arg Ile Lys Lys Thr Leu Ala Lys Met Val Glu Ser Gln
 515 520 525
 Asp Val Lys Ile
 530

366

<210> 182
 <211> 395
 <212> PRT
 <213> Homo sapiens
 <400> 182
 1 Pro Ser Gly Lys Glu Val Leu Leu Met Gln Ala Leu Asn Thr Leu
 5 10 15
 Ser Thr Pro Glu Glu Lys Leu Ala Ala Leu Cys Lys Lys Tyr Ala Asp
 20 25 30
 Leu Leu Glu Glu Ser Arg Ser Val Gln Lys Gln Met Lys Ile Leu Gln
 35 40 45
 Lys Lys Gln Ala Gln Ile Val Lys Glu Lys Val His Leu Gln Ser Glu
 50 55 60
 His Ser Lys Ala Ile Leu Ala Arg Ser Lys Leu Glu Ser Leu Cys Arg
 65 70 75 80
 Glu Leu Gln Arg His Asn Lys Thr Leu Lys Glu Glu Asn Met Gln Gln
 85 90 95
 Ala Arg Glu Glu Glu Arg Arg Lys Glu Ala Thr Ala His Phe Gln
 100 105 110
 Ile Thr Leu Asn Glu Ile Gln Ala Gln Leu Glu Gln His Asp Ile His
 115 120 125
 Asn Ala Lys Leu Arg Gln Glu Asn Ile Glu Leu Gly Glu Lys Leu Lys
 130 135 140
 Lys Leu Ile Glu Gln Tyr Ala Leu Arg Glu Glu His Ile Asp Lys Val
 145 150 155 160
 Phe Lys His Lys Glu Leu Gln Gln Leu Val Val Asp Ala Lys Leu Gln
 165 170 175
 Gln Thr Thr Gln Leu Ile Lys Glu Ala Asp Glu Lys His Gln Arg Glu
 180 185 190
 Arg Glu Phe Leu Leu Lys Glu Ala Thr Glu Ser Arg His Lys Tyr Glu
 195 200 205
 Gln Met Lys Gln Gln Glu Val Gln Leu Lys Gln Gln Leu Ser Leu Tyr
 210 215 220
 Met Asp Lys Phe Glu Glu Phe Gln Thr Thr Met Ala Lys Ser Asn Glu
 225 230 235 240
 Leu Phe Thr Thr Phe Arg Gln Glu Met Glu Lys Met Thr Lys Lys Ile
 245 250 255
 Lys Lys Leu Glu Lys Glu Thr Ile Ile Trp Arg Thr Lys Trp Glu Asn
 260 265 270
 Asn Asn Lys Ala Leu Leu Gln Met Ala Glu Glu Lys Thr Val Arg Asp
 275 280 285
 Lys Glu Tyr Lys Ala Leu Gln Ile Lys Leu Glu Arg Leu Glu Lys Leu

367

290 300
 Cys Arg Ala Leu Gln Thr Glu Arg Asn Glu Leu Asn Glu Lys Val Glu 320
 305 310 315
 Val Leu Lys Glu Gln Val Ser Ile Lys Ala Ala Ile Lys Ala Ala Asn 335
 325 330
 Arg Asp Leu Ala Thr Pro Val Met Gln Pro Cys Thr Ala Leu Asp Ser 350
 340 345
 His Lys Glu Leu Asn Thr Ser Ser Lys Arg Ala Leu Gly Ala His Leu 365
 355 360
 Glu Ala Glu Pro Lys Ser Gln Arg Ser Ala Val Gln Lys Pro Pro Ser 380
 370 375
 Thr Gly Ser Ala Pro Ala Ile Glu Ser Val Asp 395
 385 390
 <210> 183
 <211> 356
 <212> PRT
 <213> Homo sapiens
 <400> 183
 Ala Leu Cys Lys Lys Tyr Ala Glu Leu Leu Glu His Arg Asn Ser 15
 1 5 10
 Gln Lys Gln Met Lys Leu Leu Gln Lys Lys Gln Ser Gln Leu Val Gln 30
 20 25
 Glu Lys Asp His Leu Arg Gly Glu His Ser Lys Ala Val Leu Ala Arg 45
 35 40
 Ser Lys Leu Glu Ser Leu Cys Arg Glu Leu Gln Arg His Asn Arg Ser 60
 50 55
 Leu Lys Glu Glu Gly Val Gln Arg Ala Arg Glu Glu Glu Lys Arg 80
 65 70 75
 Lys Glu Val Thr Ser His Phe Gln Val Thr Leu Asn Asp Ile Gln Leu 95
 85 90
 Gln Met Glu Gln His Asn Glu Arg Asn Ser Lys Leu Arg Gln Glu Asn 110
 100 105
 Met Glu Leu Ala Glu Arg Leu Lys Lys Leu Ile Glu Gln Tyr Glu Leu 125
 115 120
 Arg Glu Glu His Ile Asp Lys Val Phe Lys His Lys Asp Leu Gln Gln 140
 130 135
 Gln Leu Val Asp Ala Lys Leu Gln Gln Ala Gln Glu Met Leu Lys Glu 160
 145 150 155
 Ala Glu Glu Arg His Gln Arg Glu Lys Asp Phe Leu Leu Lys Glu Ala 175
 165 170
 Val Glu Ser Gln Arg Met Cys Glu Leu Met Lys Gln Gln Glu Thr His 190
 180 185

368

Leu Lys Gln Gln Leu Ala Leu Tyr Thr Glu Lys Phe Glu Glu Phe Gln 205
 195 200
 Asn Thr Leu Ser Lys Ser Ser Glu Val Phe Thr Thr Phe Lys Gln Glu 220
 210 215
 Met Glu Lys Met Thr Lys Lys Ile Lys Lys Leu Glu Lys Glu Thr Thr 240
 225 230 235
 Met Tyr Arg Ser Arg Trp Glu Ser Ser Asn Lys Ala Leu Leu Glu Met 255
 245 250
 Ala Glu Glu Lys Thr Val Arg Asp Lys Glu Leu Glu Gly Leu Gln Val 270
 260 265
 Lys Ile Gln Arg Leu Glu Lys Leu Cys Arg Ala Leu Gln Thr Glu Arg 285
 275 280
 Asn Asp Leu Asn Lys Arg Val Gln Asp Leu Ser Ala Gly Gly Gln Gly 300
 290 295
 Ser Leu Thr Asp Ser Gly Pro Glu Arg Arg Pro Glu Gly Pro Gly Ala 320
 305 310 315
 Gln Ala Pro Ser Ser Pro Arg Val Thr Glu Ala Pro Cys Tyr Pro Gly 335
 325 330
 Ala Pro Ser Thr Glu Ala Ser Gly Gln Thr Gly Pro Gln Glu Pro Thr 350
 340 345
 Ser Ala Arg Ala 355
 <210> 184
 <211> 497
 <212> PRT
 <213> Homo sapiens
 <400> 184
 Met Asp Pro Leu Glu Gly Ala Pro Ser Gln Phe Val Asp Val Asp Thr Leu 15
 1 5 10
 Pro Ser Trp Gly Asp Ser Cys Gln Asp Glu Leu Asn Ser Ser Asp Thr 30
 20 25
 Thr Ala Glu Ile Phe Gln Glu Asp Thr Val Arg Ser Pro Phe Leu Tyr 45
 35 40
 Asn Lys Asp Val Asn Gly Lys Val Val Leu Trp Lys Gly Asp Val Ala 60
 50 55
 Leu Leu Asn Cys Thr Ala Ile Val Asn Thr Ser Asn Glu Ser Leu Thr 80
 65 70 75
 Asp Lys Asn Pro Val Ser Glu Ser Ile Phe Met Leu Ala Gly Pro Asp 95
 85 90
 Leu Lys Glu Asp Leu Gln Lys Leu Lys Gly Cys Arg Thr Gly Glu Ala 110
 100 105
 Lys Leu Thr Lys Gly Phe Asn Leu Ala Ala Arg Phe Ile Ile His Thr 125
 115

369

Val Gly Pro Lys Tyr Lys Ser Arg Tyr Arg Thr Ala Ala Glu Ser Ser
130 135 140
Leu Tyr Ser Cys Tyr Arg Asn Val Leu Glu Ala Lys Glu Gln Ser
145 150 155 160
Met Ser Ser Val Gly Phe Cys Val Ile Asn Ser Ala Lys Arg Gly Tyr
165 170 175
Pro Leu Glu Asp Ala Thr His Ile Ala Leu Arg Thr Val Arg Arg Phe
180 185 190
Leu Glu Ile His Gly Glu Thr Ile Glu Lys Val Val Phe Ala Val Ser
195 200 205
Asp Leu Glu Glu Gly Thr Tyr Gln Lys Leu Leu Pro Leu Tyr Phe Pro
210 215 220
Arg Ser Leu Lys Glu Glu Asn Arg Ser Leu Pro Tyr Leu Pro Ala Asp
225 230 235 240
Ile Gly Asn Ala Glu Gly Glu Pro Val Val Pro Glu Arg Gln Ile Arg
245 250 255
Ile Ser Glu Lys Pro Gly Ala Pro Glu Asp Asn Gln Glu Glu Asp
260 265 270
Glu Gly Leu Gly Val Asp Leu Ser Phe Ile Gly Ser His Ala Phe Ala
275 280 285
Arg Met Glu Gly Asp Ile Asp Lys Gln Arg Lys Leu Ile Leu Gln Gly
290 295 300
Gln Leu Ser Glu Ala Ala Leu Gln Lys Gln His Gln Arg Asn Tyr Asn
305 310 315 320
Arg Trp Leu Cys Gln Ala Arg Ser Glu Asp Leu Ser Asp Ile Ala Ser
325 330 335
Leu Lys Ala Leu Tyr Gln Thr Gly Val Asp Asn Cys Gly Arg Thr Val
340 345 350
Met Val Val Val Gly Arg Asn Ile Pro Val Thr Leu Ile Asp Met Asp
355 360 365
Lys Ala Leu Leu Tyr Phe Ile His Val Met Asp His Ile Ala Val Lys
370 375 380
Glu Tyr Val Leu Val Tyr Phe His Thr Leu Thr Ser Glu Tyr Asn His
385 390 395 400
Leu Asp Ser Asp Phe Leu Lys Lys Leu Tyr Asp Val Val Asp Val Lys
405 410 415
Tyr Lys Arg Asn Leu Lys Ala Val Tyr Phe Val His Pro Thr Phe Arg
420 425 430
Ser Lys Val Ser Thr Trp Phe Phe Thr Thr Phe Ser Val Ser Gly Leu
435 440 445
Lys Asp Lys Ile His His Val Asp Ser Leu His Gln Leu Phe Ser Ala

370

Ile Ser Pro Glu Gln Ile Asp Phe Pro Pro Phe Val Leu Glu Tyr Asp
465 470 475 480
Ala Arg Glu Asn Gly Pro Tyr Tyr Thr Ser Tyr Pro Pro Ser Pro Asp
485 490 495
Leu
<210> 185
<211> 105
<212> PRT
<213> Homo sapiens
<400> 185
Met Val Lys Gln Ile Glu Ser Lys Thr Ala Phe Gln Glu Ala Leu Asp
1 5 10 15
Ala Ala Gly Asp Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys
20 25 30
Gly Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Ser Glu Lys
35 40 45
Tyr Ser Asn Val Ile Phe Leu Glu Val Asp Val Asp Asp Cys Gln Asp
50 55 60
Val Ala Ser Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Phe
65 70 75 80
Lys Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys
85 90 95
Leu Glu Ala Thr Ile Asn Glu Leu Val
100 105
<210> 186
<211> 3038
<212> PRT
<213> Homo sapiens
<400> 186
Met Lys Ala Met Asp Val Leu Pro Ile Leu Lys Glu Lys Val Ala Tyr
1 5 10 15
Leu Ser Gly Gly Arg Asp Lys Arg Gly Gly Pro Ile Leu Thr Phe Pro
20 25 30
Ala Arg Ser Asn His Asp Arg Ile Arg Gln Glu Asp Leu Arg Arg Leu
35 40 45
Ile Ser Tyr Leu Ala Cys Ile Pro Ser Glu Glu Val Cys Lys Arg Gly
50 55 60
Phe Thr Val Ile Val Asp Met Arg Gly Ser Lys Trp Asp Ser Ile Lys
65 70 75 80
Pro Leu Leu Lys Ile Leu Gln Glu Ser Phe Pro Cys Cys Ile His Val
85 90 95

371

Ala Leu Ile Ile Lys Pro Asp Asn Phe Trp Gln Lys Gln Arg Thr Asn
100 105 110
Phe Gly Ser Ser Lys Phe Glu Phe Glu Thr Asn Met Val Ser Leu Glu
115 120 125
Gly Leu Thr Lys Lys Val Val Asp Pro Ser Gln Leu Thr Trp Glu Phe Asp
130 135 140
Gly Cys Leu Glu Tyr Asn His Glu Glu Trp Ile Glu Ile Arg Val Ala
145 150 155 160
Phe Glu Asp Tyr Ile Ser Asn Ala Thr His Met Leu Ser Arg Leu Glu
165 170 175
Glu Leu Gln Asp Ile Leu Ala Lys Lys Glu Leu Pro Gln Asp Leu Glu
180 185 190
Gly Ala Arg Asn Met Ile Glu Glu His Ser Gln Leu Lys Lys Val
195 200 205
Ile Lys Ala Pro Ile Glu Asp Leu Asp Leu Glu Gly Gln Lys Leu Leu
210 215 220
Gln Arg Ile Gln Ser Ser Glu Ser Phe Pro Lys Lys Asn Ser Gly Ser
225 230 235 240
Gly Asn Ala Asp Leu Gln Asn Leu Leu Pro Lys Val Ser Thr Met Leu
245 250 255
Asp Arg Leu His Ser Thr Arg Gln His Leu His Gln Met Trp His Val
260 265 270
Arg Lys Leu Lys Leu Asp Gln Cys Phe Gln Leu Arg Leu Phe Glu Gln
275 280 285
Asp Ala Glu Lys Met Phe Asp Trp Ile Thr His Asn Lys Gly Leu Phe
290 295 300
Leu Asn Ser Tyr Thr Glu Ile Gly Thr Ser His Pro His Ala Met Glu
305 310 315 320
Leu Gln Thr Gln His Asn His Phe Ala Met Asn Cys Met Asn Val Tyr
325 330 335
Val Asn Ile Asn Arg Ile Met Ser Val Ala Asn Arg Leu Val Glu Ser
340 345 350
Gly His Tyr Ala Ser Gln Gln Ile Arg Gln Ile Ala Ser Gln Leu Glu
355 360 365
Gln Glu Trp Lys Ala Phe Ala Ala Leu Asp Glu Arg Ser Thr Leu
370 375 380
Leu Asp Met Ser Ser Ile Phe His Gln Lys Ala Glu Lys Tyr Met Ser
385 390 395 400
Asn Val Asp Ser Trp Cys Lys Ala Cys Gly Glu Val Asp Leu Pro Ser
405 410 415
Glu Leu Gln Asp Leu Glu Asp Ala Ile His His His Gln Gly Ile Tyr
420 425 430

372

Glu His Ile Thr Leu Ala Tyr Ser Glu Val Ser Gln Asp Gly Lys Ser
435 440 445
Leu Leu Asp Lys Leu Gln Arg Pro Leu Thr Pro Gly Ser Ser Asp Ser
450 455 460
Leu Thr Ala Ser Ala Asn Tyr Ser Lys Ala Val His His Val Leu Asp
465 470 475 480
Val Ile His Glu Val Leu His His Gln Arg His Val Arg Thr Ile Trp
485 490 495
Gln His Arg Lys Val Arg Leu His Gln Arg Leu Gln Leu Cys Val Phe
500 505 510
Gln Gln Glu Val Gln Gln Val Leu Asp Trp Ile Glu Asn His Gly Glu
515 520 525
Ala Phe Leu Ser Lys His Thr Gly Val Gly Lys Ser Leu His Arg Ala
530 535 540
Arg Ala Leu Gln Lys Arg His Glu Asp Phe Glu Glu Val Ala Gln Asn
545 550 555 560
Thr Tyr Thr Asn Ala Asp Lys Leu Leu Glu Ala Ala Glu Gln Leu Ala
565 570 575
Gln Thr Gly Glu Cys Asp Pro Glu Glu Ile Tyr Gln Ala Ala His Gln
580 585 590
Leu Glu Asp Arg Ile Gln Asp Phe Val Arg Arg Val Glu Gln Arg Lys
595 600 605
Ile Leu Leu Asp Met Ser Val Ser Phe His Thr His Val Lys Glu Leu
610 615 620
Trp Thr Trp Leu Glu Glu Leu Gln Lys Glu Leu Asp Asp Val Tyr
625 630 635 640
Ala Glu Ser Val Glu Ala Val Gln Asp Leu Ile Lys Arg Phe Gly Gln
645 650 655
Gln Gln Gln Thr Thr Leu Gln Val Thr Val Asn Val Ile Lys Glu Gly
660 665 670
Glu Asp Leu Ile Gln Gln Leu Arg Asp Ser Ala Ile Ser Ser Asn Lys
675 680 685
Thr Pro His Asn Ser Ser Ile Asn His Ile Glu Thr Val Leu Gln Gln
690 695 700
Leu Asp Glu Ala Gln Ser Gln Met Glu Glu Leu Phe Gln Glu Arg Lys
705 710 715 720
Ile Lys Leu Glu Leu Phe Leu His Val Arg Ile Phe Glu Arg Asp Ala
725 730 735
Ile Asp Ile Ile Ser Asp Leu Glu Ser Trp Asn Asp Glu Leu Ser Gln
740 745 750
Gln Met Asn Asp Phe Asp Thr Glu Asp Leu Thr Ile Ala Glu Gln Arg
755 760 765 770 775 780 785 790 795 800 805 810 815 820 825 830 835 840 845 850 855 860 865 870 875 880 885 890 895 900 905 910 915 920 925 930 935 940 945 950 955 960 965 970 975 980 985 990 995

373

755 760 765
 Leu Gln His His Ala Asp Lys Ala Leu Thr Met Asn Asn Leu Thr Phe 780
 770 775
 Asp Val Ile His Gln Gly Gln Asp Leu Leu Gln Tyr Val Asn Glu Val 800
 785 790 795
 Gln Ala Ser Gly Val Glu Leu Leu Cys Asp Arg Asp Val Asp Met Ala 815
 805 810
 Thr Arg Val Gln Asp Leu Leu Glu Phe Leu His Glu Lys Gln Gln Glu 830
 820 825
 Leu Asp Leu Ala Ala Glu Gln His Arg Lys His Leu Glu Gln Cys Val 845
 835 840
 Gln Leu Arg His Leu Gln Ala Glu Val Lys Gln Val Leu Gly Trp Ile 860
 850 855
 Arg Asn Gly Glu Ser Met Leu Asn Ala Gly Leu Ile Thr Ala Ser Ser 880
 865 870 875
 Leu Gln Glu Ala Glu Gln Leu Gln Arg Glu His Glu Gln Phe Gln His 895
 885 890
 Ala Ile Glu Lys Thr His Gln Ser Ala Leu Gln Val Gln Gln Lys Ala 910
 900 905
 Glu Ala Met Leu Gln Ala Asn His Tyr Asp Met Asp Met Ile Arg Asp 925
 915 920
 Cys Ala Glu Lys Val Ala Ser His Trp Gln Gln Leu Met Leu Lys Met 940
 930 935
 Glu Asp Arg Leu Lys Leu Val Asn Ala Ser Val Ala Phe Tyr Lys Thr 960
 945 950 955
 Ser Glu Gln Val Cys Ser Val Leu Glu Ser Leu Glu Gln Glu Tyr Lys 975
 965 970
 Arg Glu Glu Asp Trp Cys Gly Ala Asp Lys Leu Gly Pro Asn Ser 990
 980 985
 Glu Thr Asp His Val Thr Pro Met Ile Ser Lys His Leu Glu Gln Lys 1005
 995 1000
 Glu Ala Phe Leu Lys Ala Cys Thr Leu Ala Arg Arg Asn Ala Asp 1020
 1010 1015
 Val Phe Leu Lys Tyr Leu His Arg Asn Ser Val Asn Met Pro Gly 1035
 1025 1030
 Met Val Thr His Ile Lys Ala Pro Glu Gln Gln Val Lys Asn Ile 1050
 1040 1045
 Leu Asn Glu Leu Phe Gln Arg Glu Asn Arg Val Leu His Tyr Trp 1065
 1055 1060
 Thr Met Arg Lys Arg Arg Leu Asp Gln Cys Gln Gln Tyr Val Val 1080
 1070 1075

Phe Glu Arg Ser Ala Lys Gln Ala Leu Glu Trp Ile His Asp Asn 1095
 1085 1090
 Gly Glu Phe Tyr Leu Ser Thr His Thr Ser Thr Gly Ser Ser Ile 1110
 1100 1105
 Gln His Thr Gln Glu Leu Leu Lys Glu His Glu Glu Phe Gln Ile 1125
 1115 1120
 Thr Ala Lys Gln Thr Lys Glu Arg Val Lys Leu Leu Ile Gln Leu 1140
 1130 1135
 Ala Asp Gly Phe Cys Glu Lys Gly His Ala His Ala Ala Glu Ile 1155
 1145 1150
 Lys Lys Cys Val Thr Ala Val Asp Lys Arg Tyr Arg Asp Phe Ser 1170
 1160 1165
 Leu Arg Met Glu Lys Tyr Arg Thr Ser Leu Glu Lys Ala Leu Gly 1185
 1175 1180
 Ile Ser Ser Asp Ser Asn Lys Ser Ser Lys Ser Leu Gln Leu Asp 1200
 1190 1195
 Ile Ile Pro Ala Ser Ile Pro Gly Ser Glu Val Lys Leu Arg Asp 1215
 1205 1210
 Ala Ala His Glu Leu Asn Glu Glu Lys Arg Lys Ser Ala Arg Arg 1230
 1220 1225
 Lys Glu Phe Ile Met Ala Glu Leu Ile Gln Thr Glu Lys Ala Tyr 1245
 1235 1240
 Val Arg Asp Leu Arg Glu Cys Met Asp Thr Tyr Leu Trp Glu Met 1260
 1250 1255
 Thr Ser Gly Val Glu Glu Ile Pro Pro Gly Ile Val Asn Lys Glu 1275
 1265 1270
 Leu Ile Ile Phe Gly Asn Met Gln Glu Ile Tyr Glu Phe His Asn 1290
 1280 1285
 Asn Ile Phe Leu Lys Glu Leu Glu Lys Tyr Glu Gln Leu Pro Glu 1305
 1295 1300
 Asp Val Gly His Cys Phe Val Thr Trp Ala Asp Lys Phe Gln Met 1320
 1310 1315
 Tyr Val Thr Tyr Cys Lys Asn Lys Pro Asp Ser Thr Gln Leu Ile 1335
 1325 1330
 Leu Glu His Ala Gly Ser Tyr Phe Asp Glu Ile Gln Gln Arg His 1350
 1340 1345
 Gly Leu Ala Asn Ser Ile Ser Ser Tyr Leu Ile Lys Pro Val Gln 1365
 1355 1360
 Arg Ile Thr Lys Tyr Gln Leu Leu Leu Lys Glu Leu Leu Thr Cys 1380
 1370 1375
 Cys Glu Glu Gly Lys Gly Glu Ile Lys Asp Gly Leu Glu Val Met 1395
 1385 1390

Leu Ser Val Pro Lys Arg Ala Asn Asp Ala Met His Leu Ser Met
 1400 1405 1410
 Leu Glu Gly Phe Asp Glu Asn Ile Glu Ser Gln Gly Glu Leu Ile
 1415 1420 1425
 Leu Gln Glu Ser Phe Gln Val Trp Asp Pro Lys Thr Leu Ile Arg
 1430 1435 1440
 Lys Gly Arg Glu Arg His Leu Phe Leu Phe Glu Met Ser Leu Val
 1445 1450 1455
 Phe Ser Lys Glu Val Lys Asp Ser Ser Gly Arg Ser Lys Tyr Leu
 1460 1465 1470
 Tyr Lys Ser Lys Leu Phe Thr Ser Glu Leu Gly Val Thr Glu His
 1475 1480 1485
 Val Glu Gly Asp Pro Cys Lys Phe Ala Leu Trp Val Gly Arg Thr
 1490 1495 1500
 Pro Thr Ser Asp Asn Lys Ile Val Leu Lys Ala Ser Ser Ile Glu
 1505 1510 1515
 Asn Lys Gln Asp Trp Ile Lys His Ile Arg Glu Val Ile Gln Glu
 1520 1525 1530
 Arg Thr Ile His Leu Lys Gly Ala Leu Lys Glu Pro Ile His Ile
 1535 1540 1545
 Pro Lys Thr Ala Pro Ala Thr Arg Gln Lys Gly Arg Asp Gly
 1550 1555 1560
 Glu Asp Leu Asp Ser Gln Gly Asp Gly Ser Ser Gln Pro Asp Thr
 1565 1570 1575
 Ile Ser Ile Ala Ser Arg Thr Ser Gln Asn Thr Leu Asp Ser Asp
 1580 1585 1590
 Lys Leu Ser Gly Gly Cys Glu Leu Thr Val Val Ile His Asp Phe
 1595 1600 1605
 Thr Ala Cys Asn Ser Asn Glu Leu Thr Ile Arg Arg Gly Gln Thr
 1610 1615 1620
 Val Glu Val Leu Glu Arg Pro His Asp Lys Pro Asp Trp Cys Leu
 1625 1630 1635
 Val Arg Thr Thr Asp Arg Ser Pro Ala Ala Glu Gly Leu Val Pro
 1640 1645 1650
 Cys Gly Ser Leu Cys Ile Ala His Ser Arg Ser Ser Met Glu Met
 1655 1660 1665
 Glu Gly Ile Phe Asn His Lys Asp Ser Leu Ser Val Ser Ser Asn
 1670 1675 1680
 Asp Ala Ser Pro Pro Ala Ser Val Ala Ser Leu Gln Pro His Met
 1685 1690 1695
 Ile Gly Ala Gln Ser Ser Pro Gly Pro Lys Arg Pro Gly Asn Thr

1700 1705 1710
 Leu Arg Lys Trp Leu Thr Ser Pro Val Arg Arg Leu Ser Ser Gly
 1715 1720 1725
 Lys Ala Asp Gly His Val Lys Lys Leu Ala His Lys His Lys Lys
 1730 1735 1740
 Ser Arg Glu Val Arg Lys Ser Ala Asp Ala Gly Ser Gln Lys Asp
 1745 1750 1755
 Ser Asp Asp Ser Ala Ala Thr Pro Gln Asp Glu Thr Val Glu Glu
 1760 1765 1770
 Arg Gly Arg Asn Glu Gly Leu Ser Ser Gly Thr Leu Ser Lys Ser
 1775 1780 1785
 Ser Ser Ser Gly Met Gln Ser Cys Gly Glu Glu Gly Glu Glu
 1790 1795 1800
 Gly Ala Asp Ala Val Pro Leu Pro Pro Pro Met Ala Ile Gln Gln
 1805 1810 1815
 His Ser Leu Leu Gln Pro Asp Ser Gln Asp Asp Lys Ala Ser Ser
 1820 1825 1830
 Arg Leu Leu Val Arg Pro Thr Ser Ser Glu Thr Pro Ser Ala Ala
 1835 1840 1845
 Glu Leu Val Ser Ala Ile Glu Glu Leu Val Lys Ser Lys Met Ala
 1850 1855 1860
 Leu Glu Asp Arg Pro Ser Ser Leu Leu Val Asp Gln Gly Asp Ser
 1865 1870 1875
 Ser Ser Pro Ser Phe Asn Pro Ser Asp Asn Ser Leu Leu Ser Ser
 1880 1885 1890
 Ser Ser Pro Ile Asp Glu Met Glu Glu Arg Lys Ser Ser Ser Leu
 1895 1900 1905
 Lys Arg Arg His Tyr Val Leu Gln Glu Leu Val Thr Glu Arg
 1910 1915 1920
 Asp Tyr Val Arg Asp Leu Gly Tyr Val Val Glu Gly Tyr Met Ala
 1925 1930 1935
 Leu Met Lys Glu Asp Gly Val Pro Asp Asp Met Lys Gly Lys Asp
 1940 1945 1950
 Lys Ile Val Phe Gly Asn Ile His Gln Ile Tyr Asp Trp His Arg
 1955 1960 1965
 Asp Phe Phe Leu Gly Glu Leu Glu Lys Cys Leu Glu Asp Pro Glu
 1970 1975 1980
 Lys Leu Gly Ser Leu Phe Val Lys His Glu Arg Arg Leu His Met
 1985 1990 1995
 Tyr Ile Ala Tyr Cys Gln Asn Lys Pro Lys Ser Glu His Ile Val
 2000 2005 2010

Ser Glu Tyr Ile Asp Thr Phe Phe Glu Asp Leu Lys Gln Arg Leu 2025
 2015
 Gly His Arg Leu Gln Leu Thr Asp Leu Leu Ile Lys Pro Val Gln 2040
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 Arg Ile Met Lys Tyr Gln Leu Leu Leu Lys Asp Phe Leu Lys Tyr 2055
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 Ser Lys Lys Ala Ser Leu Asp Thr Ser Glu Leu Glu Arg Ala Val 2070
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 Glu Val Met Cys Ile Val Pro Arg Arg Cys Asn Asp Met Met Asn 2085
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 Val Gly Arg Leu Gln Gly Phe Asp Gly Lys Ile Val Ala Gln Gly 2100
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 Lys Leu Leu Leu Gln Asp Thr Phe Leu Val Thr Asp Gln Asp Ala 2115
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 Gly Leu Leu Pro Arg Cys Arg Glu Arg Arg Ile Phe Leu Phe Glu 2130
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 Gln Ile Val Ile Phe Ser Glu Pro Leu Asp Lys Lys Lys Gly Phe 2145
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 Ser Met Pro Gly Phe Leu Phe Lys Asn Ser Ile Lys Val Ser Cys 2160
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 Ser Ser Pro Ser Val Arg Gln Thr Trp Ile His Glu Ile Asn 2205
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 Pro Ile Glu Tyr Gln Arg Asn His Ser Gly Gly Gly Gly Gly 2235
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 Gly Ser Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly 2250
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 Ala Pro Ser Gly Gly Ser Gly His Ser Gly Gly Pro Ser Ser Cys 2265
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 Gly Gly Ala Pro Ser Thr Ser Arg Ser Arg Pro Ser Arg Ile Pro 2280
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 Gln Pro Val Arg His His Pro Pro Val Leu Val Ser Ser Ala Ala 2295
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 Gly Pro Ser Leu Pro Pro Gly Ala Ala Pro Glu Ala Gly Pro 2325
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 Ser Ala Val Pro Ser Leu Gly Lys Glu Pro Phe Pro Pro Ser Ser 2415
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 Pro Leu Gln Lys Gly Gly Ser Phe Thr Ser Ser Ile Pro Ala Ser 2430
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 Pro Ala Ser Arg Pro Gly Ser Phe Thr Phe Pro Gly Asp Ser Asp 2445
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 Ser Leu Gln Arg Gln Thr Pro Arg His Ala Ala Pro Gly Lys Asp 2460
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 Thr Asp Arg Met Ser Thr Cys Ser Ser Ala Ser Glu Gln Ser Val 2475
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 Gln Ser Thr Gln Ser Asn Gly Ser Glu Ser Ser Ser Ser Asn 2490
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 His Thr Ser Ala Val Ile Val Glu Asn Pro Asp Gly Thr Leu Lys 2565
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 Gly Tyr Arg Lys Ser Arg Glu Gly Leu Ser Asn Lys Val Ser Val 2610
 2600
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 2735 Ser Val Val Lys Lys Cys Asp Gln Lys Gly Thr Lys Arg Ala Val 2745
 2750 Ala Thr Lys Phe Val Asn Lys Lys Leu Met Lys Arg Asp Gln Val 2760
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 2825 Glu Val Leu Glu Ala Val Arg Tyr Leu His Asn Cys Arg Ile Ala 2835
 2840 His Leu Asp Leu Lys Pro Glu Asn Ile Leu Val Asp Glu Ser Leu 2850
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 2870 Leu Asn Thr Thr Tyr Tyr Ile His Gln Leu Leu Gly Asn Pro Glu 2880
 2885 Phe Ala Ala Pro Glu Ile Ile Leu Gly Asn Pro Val Ser Leu Thr 2895
 2900 Ser Asp Thr Trp Ser Val Gly Val Leu Thr Tyr Val Leu Leu Ser 2910
 2915 Gly Val Ser Pro Phe Leu Asp Asp Ser Val Glu Glu Thr Cys Leu 2925
 2930

380

Asn Ile Cys Arg Leu Asp Phe Ser Phe Pro Asp Asp Tyr Phe Lys 2945
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 Ser Asp Val Leu Pro Ile Leu Lys Glu Lys Val Ala Phe Val Ser Gly 35
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 Gly Arg Asp Lys Arg Gly Gly Pro Ile Leu Thr Phe Pro Ala Arg Ser 50
 55 60
 Asn His Asp Arg Ile Arg Gln Glu Asp Leu Arg Lys Leu Val Thr Tyr 65
 70 75 80
 Leu Ala Ser Val Pro Ser Glu Asp Val Cys Lys Arg Gly Phe Thr Val 85
 90 95
 Ile Ile Asp Met Arg Gly Ser Lys Trp Asp Leu Ile Lys Pro Leu Leu 100
 105 110
 Lys Thr Leu Gln Glu Ala Phe Pro Ala Glu Ile His Val Ala Leu Ile 115
 120 125
 Ile Lys Pro Asp Asn Phe Trp Gln Lys Gln Lys Thr Asn Phe Gly Ser 130
 135 140
 Ser Lys Phe Ile Phe Glu Thr Ser Met Val Ser Val Glu Gly Leu Thr 145
 150 155 160
 Lys Leu Val Asp Pro Ser Gln Leu Thr Glu Glu Phe Asp Gly Ser Leu 165
 170 175
 Asp Tyr Asn His Glu Glu Trp Ile Glu Leu Arg Leu Ser Leu Glu 180
 185 190

381

Phe Phe Asn Ser Ala Val His Leu Leu Ser Arg Leu Glu Asp Leu Gln
 195 200 205
 Glu Met Leu Ala Arg Lys Glu Phe Pro Val Asp Val Glu Gly Ser Arg
 210 215 220
 Arg Leu Ile Asp Glu His Thr Gln Leu Lys Lys Lys Val Leu Lys Ala
 225 230 235 240
 Pro Val Glu Leu Asp Arg Glu Gly Gln Arg Leu Leu Gln Cys Ile
 245 250 255
 Arg Cys Ser Asp Gly Phe Ser Gly Arg Asn Cys Ile Pro Gly Ser Ala
 260 265 270
 Asp Phe Gln Ser Leu Val Pro Lys Ile Thr Ser Leu Leu Asp Lys Leu
 275 280 285
 His Ser Thr Arg Gln His Leu His Gln Met Trp His Val Arg Lys Leu
 290 295 300
 Lys Leu Asp Gln Cys Phe Gln Leu Arg Leu Phe Glu Gln Asp Ala Glu
 305 310 315 320
 Lys Met Phe Asp Trp Ile Ser His Asn Lys Glu Leu Phe Leu Gln Ser
 325 330 335
 His Thr Glu Ile Gly Val Ser Tyr Gln Tyr Ala Leu Asp Leu Gln Thr
 340 345 350
 Gln His Asn His Phe Ala Met Asn Ser Met Asn Ala Tyr Val Asn Ile
 355 360 365
 Asn Arg Ile Met Ser Val Ala Ser Arg Leu Ser Glu Ala Gly His Tyr
 370 375 380
 Ala Ser Gln Gln Ile Lys Gln Ile Ser Thr Gln Leu Asp Gln Glu Trp
 385 390 395 400
 Lys Ser Phe Ala Ala Leu Asp Glu Arg Ser Thr Ile Leu Ala Met
 405 410 415
 Ser Ala Val Phe His Gln Lys Ala Glu Gln Phe Leu Ser Gly Val Asp
 420 425 430
 Ala Trp Cys Lys Met Cys Ser Glu Gly Gly Leu Pro Ser Glu Met Gln
 435 440 445
 Asp Leu Glu Leu Ala Ile His His His Gln Thr Leu Tyr Glu Gln Val
 450 455 460
 Thr Gln Ala Tyr Thr Glu Val Ser Gln Asp Gly Lys Ala Leu Leu Asp
 465 470 475 480
 Val Leu Gln Arg Pro Leu Ser Pro Gly Asn Ser Glu Ser Leu Thr Ala
 485 490 495
 Thr Ala Asn Tyr Ser Lys Ala Val His Gln Val Leu Asp Val Val His
 500 505 510
 Glu Val Leu His His Gln Arg Arg Leu Glu Ser Ile Trp Gln His Arg

515 520 525
 Lys Val Arg Leu His Gln Arg Leu Gln Leu Cys Val Phe Gln Gln Asp
 530 535 540
 Val Gln Gln Val Leu Asp Trp Ile Glu Asn His Gly Glu Ala Phe Leu
 545 550 555 560
 Ser Lys His Thr Gly Val Gly Lys Ser Leu His Arg Ala Arg Ala Leu
 565 570 575
 Gln Lys Arg His Asp Asp Phe Glu Glu Val Ala Gln Asn Thr Tyr Thr
 580 585 590
 Asn Ala Asp Lys Leu Leu Glu Ala Ala Glu Gln Leu Ala Gln Thr Gly
 595 600 605
 Glu Cys Asp Pro Glu Glu Ile Tyr Lys Ala Ala Arg His Leu Glu Val
 610 615 620
 Arg Ile Gln Asp Phe Val Arg Arg Val Glu Gln Arg Lys Leu Leu
 625 630 635 640
 Asp Met Ser Val Ser Phe His Thr His Thr Lys Glu Leu Trp Thr Trp
 645 650 655
 Met Glu Asp Leu Gln Lys Glu Met Leu Glu Asp Val Cys Ala Asp Ser
 660 665 670
 Val Asp Ala Val Gln Glu Leu Ile Lys Gln Phe Gln Gln Gln Thr
 675 680 685
 Ala Thr Leu Asp Ala Thr Leu Asn Val Ile Lys Glu Gly Glu Asp Leu
 690 695 700
 Ile Gln Gln Leu Arg Ser Ala Pro Pro Ser Leu Gly Glu Pro Ser Glu
 705 710 715 720
 Ala Arg Asp Ser Ala Val Ser Asn Asn Lys Thr Pro His Ser Ser Ser
 725 730 735
 Ile Ser His Ile Glu Ser Val Leu Gln Gln Leu Asp Asp Ala Gln Val
 740 745 750
 Gln Met Glu Glu Leu Phe His Glu Arg Lys Ile Lys Leu Asp Ile Phe
 755 760 765
 Leu Gln Leu Arg Ile Phe Glu Gln Tyr Thr Ile Glu Val Thr Ala Glu
 770 775 780
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 Thr Glu Asp Leu Thr Leu Ala Glu Gln Arg Leu Gln Arg His Thr Glu
 805 810 815
 Arg Lys Leu Ala Met Asn Asn Met Thr Phe Glu Val Ile Gln Gln Gly
 820 825 830
 Gln Asp Leu His Gln Tyr Ile Thr Glu Val Gln Ala Ser Gly Ile Glu
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Leu Ile Cys Glu Lys Asp Ile Asp Leu Ala Ala Gln Val Gln Glu Leu 850
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 Gln Thr His Lys Arg Leu Glu Gln Cys Leu Glu Arg His Leu Gln 880
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 Gln Lys Ala Glu Val Leu Leu Gln Ala Gly His Tyr Asp Ala Asp Ala 965
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 Ile Arg Glu Cys Ala Glu Lys Val Ala Leu His Trp Gln Gln Leu Met 980
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 Leu Lys Met Glu Asp Arg Leu Lys Leu Val Asn Ala Ser Val Ala Phe 990
 995 1000 1005
 Tyr Lys Thr Ser Glu Gln Val Cys Ser Val Leu Glu Ser Leu Glu 1010
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 Gln Glu Tyr Arg Arg Asp Glu Asp Trp Cys Gly Gly Arg Asp Lys 1025
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 Leu Gly Pro Ala Ala Glu Ile Asp His Val Ile Pro Leu Ile Ser 1040
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 Ala Arg Arg Asn Ala Glu Val Phe Leu Lys Tyr Ile His Arg Asn 1070
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 Gln Gln Val Lys Ala Ile Leu Ser Glu Leu Leu Gln Arg Glu Asn 1100
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 Arg Val Leu His Phe Trp Thr Leu Lys Lys Arg Arg Leu Asp Gln 1115
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 1135 1140
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 1150 1155
 Ser Thr Gly Glu Thr Thr Glu Glu Thr Gln Glu Leu Leu Lys Glu 1160
 1165 1170

Tyr Gly Glu Phe Arg Val Pro Ala Lys Gln Thr Lys Glu Lys Val 1175
 1180 1185
 Lys Leu Leu Ile Gln Leu Ala Asp Ser Phe Val Glu Lys Gly His 1190
 1195 1200
 Ile His Ala Thr Glu Ile Arg Lys Trp Val Thr Thr Val Asp Lys 1205
 1210 1215
 His Tyr Arg Asp Phe Ser Leu Arg Met Gly Lys Tyr Arg Tyr Ser 1220
 1225 1230
 Leu Glu Lys Ala Leu Gly Val Asn Thr Glu Asp Asn Lys Asp Leu 1235
 1240 1245
 Glu Leu Asp Ile Ile Pro Ala Ser Leu Ser Asp Arg Glu Val Lys 1250
 1255 1260
 Leu Arg Asp Ala Asn His Glu Val Asn Glu Glu Lys Arg Lys Ser 1265
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 Ala Arg Lys Lys Glu Phe Ile Met Ala Glu Leu Gln Thr Glu 1280
 1285 1290
 Lys Ala Tyr Val Arg Asp Leu His Glu Cys Leu Glu Thr Tyr Leu 1295
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 Trp Glu Met Thr Ser Gly Val Glu Glu Ile Pro Pro Gly Ile Leu 1310
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 Asn Lys Glu His Ile Ile Phe Gly Asn Ile Gln Glu Ile Tyr Asp 1325
 1330 1335
 Phe His Asn Asn Ile Phe Leu Lys Glu Leu Glu Lys Tyr Glu Gln 1340
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 Leu Pro Glu Asp Val Gly His Cys Phe Val Thr Trp Ala Asp Lys 1355
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 Phe Gln Met Tyr Val Thr Tyr Cys Lys Asn Lys Pro Asp Ser Asn 1370
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 Gln Leu Ile Leu Glu His Ala Gly Thr Phe Phe Asp Glu Ile Gln 1385
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 Gln Arg His Gly Leu Ala Asn Ser Ile Ser Ser Tyr Leu Ile Lys 1400
 1405 1410
 Pro Val Gln Arg Ile Thr Lys Tyr Gln Leu Leu Lys Glu Leu 1415
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 Leu Thr Cys Cys Glu Glu Gly Lys Gly Glu Leu Lys Asp Gly Leu 1430
 1435 1440
 Glu Val Met Leu Ser Val Pro Lys Lys Ala Asn Asp Ala Met His 1445
 1450 1455
 Val Ser Met Leu Glu Gly Phe Asp Glu Asn Leu Asp Val Gln Gly 1460
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 Glu Leu Ile Leu Gln Asp Ala Phe Gln Val Trp Asp Pro Lys Ser

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 Ser Leu Val Phe Ser Lys Glu Ile Lys Asp Ser Ser Gly His Thr
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 Lys Tyr Val Tyr Lys Asn Lys Leu Leu Thr Ser Glu Leu Gly Val
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 Thr Glu His Val Glu Gly Asp Pro Cys Lys Phe Ala Leu Trp Ser
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 35 40 45
 Tyr Asp Arg Glu Thr Gly Lys Pro Lys Gly Tyr Gly Phe Cys Glu Tyr
 50 55 60
 Glu Asp Glu Glu Thr Ala Leu Ser Ala Met Arg Asn Leu Asn Gly Arg
 65 70 75 80
 Glu Phe Ser Gly Arg Ala Leu Arg Val Asp Asn Ala Ala Ser Glu Lys
 85 90 95

386

Asn Lys Glu Glu Leu Lys Ser Leu Gly Pro Ala Ala Pro Ile Ile Asp
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 Ser Pro Tyr Gly Asp Pro Ile Asp Pro Glu Asp Ala Pro Glu Ser Ile
 115 120 125
 Thr Arg Ala Val Ala Ser Leu Pro Pro Glu Glu Met Phe Glu Leu Met
 130 135 140
 Lys Glu Met Lys Leu Cys Val Glu Asn Ser His Glu Glu Ala Arg Asn
 145 150 155 160
 Met Leu Leu Glu Asn Pro Glu Leu Ala Tyr Ala Leu Leu Glu Ala Glu
 165 170 175
 Val Val Met Arg Ile Met Asp Pro Glu Ile Ala Leu Lys Ile Leu His
 180 185 190
 Arg Lys Ile His Val Thr Pro Leu Ile Pro Gly Lys Ser Glu Ser Val
 195 200 205
 Ser Val Ser Gly Pro Gly Pro Gly Pro Gly Pro Gly Leu Cys Pro Gly
 210 215 220
 Pro Asn Val Leu Leu Asn Glu Glu Asn Pro Pro Ala Pro Glu Pro Glu
 225 230 235 240
 His Leu Ala Arg Arg Pro Val Lys Asp Ile Pro Pro Leu Met Glu Thr
 245 250 255
 Pro Ile Glu Gly Gly Ile Pro Ala Pro Gly Pro Ile Pro Ala Ala Val
 260 265 270
 Pro Gly Ala Gly Pro Gly Ser Leu Thr Pro Gly Gly Ala Met Glu Pro
 275 280 285
 Glu Leu Gly Met Pro Gly Val Gly Pro Val Pro Leu Glu Arg Gly Glu
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 Val Glu Met Ser Asp Pro Arg Ala Pro Ile Pro Arg Gly Pro Val Thr
 305 310 315 320
 Pro Gly Gly Leu Pro Pro Arg Gly Leu Leu Gly Asp Ala Pro Asn Asp
 325 330 335
 Pro Arg Gly Gly Thr Leu Leu Ser Val Thr Gly Glu Val Glu Pro Arg
 340 345 350
 Gly Tyr Leu Gly Pro Pro His Glu Gly Pro Pro Met His Ala Ser
 355 360 365
 Gly His Asp Thr Arg Gly Pro Ser Ser His Glu Met Arg Gly Gly Pro
 370 375 380
 Leu Gly Asp Pro Arg Leu Leu Ile Gly Glu Pro Arg Gly Pro Met Ile
 385 390 395 400
 Asp Glu Arg Gly Leu Pro Met Asp Gly Arg Gly Gly Arg Asp Ser Arg
 405 410 415
 Ala Met Glu Thr Arg Ala Met Glu Thr Glu Val Leu Glu Thr Arg Val
 420 425 430

387

Met Glu Arg Arg Gly Met Glu Thr Cys Ala Met Glu Thr Arg Gly Met 435 440 445
 Glu Ala Arg Gly Met Asp Ala Arg Gly Leu Glu Met Arg Gly Pro Val 450 455 460
 Pro Ser Ser Arg Gly Pro Met Thr Gly Gly Ile Gln Gly Pro Gly Pro 465 470 475 480
 Ile Asn Ile Gly Ala Gly Gly Pro Pro Gln Gly Pro Arg Gln Val Pro 485 490 495
 Gly Ile Ser Gly Val Gly Asn Pro Gly Ala Gly Met Gln Gly Thr Gly 500 505 510
 Ile Gln Gly Thr Gly Met Gln Gly Ala Gly Ile Gln Gly Gly Met 515 520 525
 Gln Gly Ala Gly Ile Gln Gly Val Ser Ile Gln Gly Gly Ile Gln 530 535 540
 Gly Gly Gly Ile Gln Gly Ala Ser Lys Gln Gly Gly Ser Gln Pro Ser 545 550 555 560
 Ser Phe Ser Pro Gly Gln Ser Gln Val Thr Pro Gln Asp Gln Glu Lys 565 570 575
 Ala Ala Leu Ile Met Gln Val Leu Gln Leu Thr Ala Asp Gln Ile Ala 580 585 590
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 Lys Asp Ile Phe Ser Glu Val Gly Pro Val Val Ser Phe Arg Leu Val 35 40 45
 Tyr Asp Arg Glu Thr Gly Lys Pro Lys Gly Tyr Gly Phe Cys Glu Tyr 50 55 60
 Gln Asp Gln Glu Thr Ala Leu Ser Ala Met Arg Asn Leu Asn Gly Arg 65 70 75 80
 Glu Phe Ser Gly Arg Ala Leu Arg Val Asp Asn Ala Ala Ser Glu Lys 85 90 95
 Asn Lys Glu Glu Leu Lys Ser Leu Gly Thr Gly Ala Pro Val Ile Glu

388

100 105 110
 Ser Pro Tyr Gly Glu Thr Ile Ser Pro Glu Asp Ala Pro Glu Ser Ile 115 120 125
 Ser Lys Ala Val Ala Ser Leu Pro Glu Gln Met Phe Glu Leu Met 130 135 140
 Lys Gln Met Lys Leu Cys Val Gln Asn Ser Pro Gln Glu Ala Arg Asn 145 150 155 160
 Met Leu Leu Gln Asn Pro Gln Leu Ala Tyr Ala Leu Leu Gln Ala Gln 165 170 175
 Val Val Met Arg Ile Val Asp Pro Glu Ile Ala Leu Lys Ile Leu His 180 185 190
 Arg Gln Thr Asn Ile Pro Thr Leu Ile Ala Gly Asn Pro Gln Pro Val 195 200 205
 His Gly Ala Gly Pro Gly Ser Gly Ser Asn Val Ser Met Asn Gln Gln 210 215 220
 Asn Pro Gln Ala Pro Gln Ala Gln Ser Leu Gly Gly Met His Val Asn 225 230 235 240
 Gly Ala Pro Pro Leu Met Gln Ala Ser Met Gln Gly Gly Val Pro Ala 245 250 255
 Pro Gly Gln Met Pro Ala Ala Val Thr Gly Pro Gly Pro Gly Ser Leu 260 265 270
 Ala Pro Gly Gly Gly Met Gln Ala Gln Val Gly Met Pro Gly Ser Gly 275 280 285
 Pro Val Ser Met Glu Arg Gly Gln Val Pro Met Gln Asp Pro Arg Ala 290 295 300
 Ala Met Gln Arg Gly Ser Leu Pro Ala Asn Val Pro Thr Pro Arg Gly 305 310 315 320
 Leu Leu Gly Asp Ala Pro Asn Asp Pro Arg Gly Gly Thr Leu Leu Ser 325 330 335
 Val Thr Gly Glu Val Glu Pro Arg Gly Tyr Leu Gly Pro Pro His Gln 340 345 350
 Gly Pro Pro Met His His Val Pro Gly His Glu Ser Arg Gly Pro Pro 355 360 365
 Pro His Glu Leu Arg Gly Gly Pro Leu Pro Glu Pro Arg Pro Leu Met 370 375 380
 Ala Glu Pro Arg Gly Pro Met Leu Asp Gln Arg Gly Pro Pro Leu Asp 385 390 395 400
 Gly Arg Gly Gly Arg Asp Pro Arg Gly Ile Asp Ala Arg Gly Met Glu 405 410 415
 Ala Arg Ala Met Glu Ala Arg Gly Leu Asp Ala Arg Gly Leu Glu Ala 420 425 430

389

Arg Ala Met Glu Ala Arg Ala Met Glu Ala Arg Ala Met Glu Ala Arg
 435 440 445
 Ala Met Glu Ala Arg Ala Met Glu Val Arg Gly Met Glu Ala Arg Gly
 450 455 460
 Met Asp Thr Arg Gly Pro Val Pro Gly Pro Arg Gly Pro Ile Pro Ser
 465 470 475 480
 Gly Met Gln Gly Pro Ser Pro Ile Asn Met Gly Ala Val Val Pro Gln
 485 490 495
 Gly Ser Arg Gln Val Pro Val Met Gln Gly Thr Gly Met Gln Gly Ala
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 Ser Ile Gln Gly Gly Ser Gln Pro Gly Gly Phe Ser Pro Gly Gln Asn
 515 520 525
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 35 40 45
 Lys Ala Arg Lys Thr Tyr Glu Arg Leu Val Ala Gln Phe Pro Ser Ser
 50 55 60
 Gly Arg Phe Trp Lys Leu Tyr Ile Glu Ala Glu Ile Lys Ala Lys Asn
 65 70 75 80
 Tyr Asp Lys Val Glu Lys Leu Phe Gln Arg Cys Leu Met Lys Val Leu
 85 90 95
 His Ile Asp Leu Trp Lys Cys Tyr Leu Ser Tyr Val Arg Glu Thr Lys
 100 105 110
 Gly Lys Leu Pro Ser Tyr Lys Glu Lys Met Ala Gln Ala Tyr Asp Phe
 115 120 125
 Ala Leu Asp Lys Ile Gly Met Glu Ile Met Ser Tyr Gln Ile Trp Val
 130 135 140

390

Asp Tyr Ile Asn Phe Leu Lys Gly Val Glu Ala Val Gly Ser Tyr Ala
 145 150 155 160
 Glu Asn Gln Arg Ile Thr Ala Val Arg Arg Val Tyr Gln Arg Gly Cys
 165 170 175
 Val Asn Pro Met Ile Asn Ile Glu Gln Leu Trp Arg Asp Tyr Asn Lys
 180 185 190
 Tyr Glu Glu Gly Ile Asn Ile His Leu Ala Lys Lys Met Ile Glu Asp
 195 200 205
 Arg Ser Arg Asp Tyr Met Asn Ala Arg Arg Val Ala Lys Glu Tyr Glu
 210 215 220
 Thr Val Met Lys Gly Leu Asp Arg Asn Ala Pro Ser Val Pro Pro Gln
 225 230 235 240
 Asn Thr Pro Gln Glu Ala Gln Gln Val Asp Met Trp Lys Tyr Ile
 245 250 255
 Gln Trp Glu Lys Ser Asn Pro Leu Arg Thr Glu Asp Gln Thr Leu Ile
 260 265 270
 Thr Lys Arg Val Met Phe Ala Tyr Glu Gln Cys Leu Leu Val Leu Gly
 275 280 285
 His His Pro Asp Ile Trp Tyr Glu Ala Ala Gln Tyr Leu Glu Gln Ser
 290 295 300
 Ser Lys Leu Leu Ala Glu Lys Gly Asp Met Asn Asn Ala Lys Leu Phe
 305 310 315 320
 Ser Asp Glu Ala Ala Asn Ile Tyr Glu Arg Ala Ile Ser Thr Leu Leu
 325 330 335
 Lys Lys Asn Met Leu Leu Tyr Phe Ala Tyr Ala Asp Tyr Glu Glu Ser
 340 345 350
 Arg Met Lys Tyr Glu Lys Val His Ser Ile Tyr Asn Arg Leu Leu Ala
 355 360 365
 Ile Glu Asp Ile Asp Pro Thr Leu Val Tyr Ile Gln Tyr Met Lys Phe
 370 375 380
 Ala Arg Arg Ala Glu Gly Ile Lys Ser Gly Arg Met Ile Phe Lys Lys
 385 390 395 400
 Ala Arg Glu Asp Thr Arg Thr Arg His His Val Tyr Val Thr Ala Ala
 405 410 415
 Leu Met Glu Tyr Tyr Cys Ser Lys Asp Lys Ser Val Ala Phe Lys Ile
 420 425 430
 Phe Glu Leu Gly Leu Lys Lys Tyr Gly Asp Ile Pro Glu Tyr Val Leu
 435 440 445
 Ala Tyr Ile Asp Tyr Leu Ser His Leu Asn Glu Asp Asn Asn Thr Arg
 450 455 460
 Val Leu Phe Glu Arg Val Leu Thr Ser Gly Ser Leu Pro Pro Glu Lys

391

465 470 475 480
 Ser Gly Glu Ile Trp Ala Arg Phe Leu Ala Phe Glu Ser Asn Ile Gly 495
 485
 Asp Leu Ala Ser Ile Leu Lys Val Glu Lys Arg Arg Phe Thr Ala Phe 510
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 Lys Glu Glu Tyr Glu Gly Lys Glu Thr Ala Leu Leu Val Asp Arg Tyr 525
 515 520
 Lys Phe Met Asp Leu Tyr Pro Cys Ser Ala Ser Glu Leu Lys Ala Leu 540
 530 540
 Gly Tyr Lys Asp Val Ser Arg Ala Lys Leu Ala Ala Ile Ile Pro Asp 560
 545 550 555
 Pro Val Val Ala Pro Ser Ile Val Pro Val Leu Lys Asp Glu Val Asp 575
 565 570
 Arg Lys Pro Glu Tyr Pro Lys Pro Asp Thr Glu Glu Met Ile Pro Phe 590
 580 585
 Gln Pro Arg His Leu Ala Pro Pro Gly Leu His Pro Val Pro Gly Gly 605
 595 600
 Val Phe Pro Val Pro Pro Ala Ala Val Val Leu Met Lys Leu Leu Pro 620
 610 615
 Pro Pro Ile Cys Phe Gln Gly Pro Phe Val Gln Val Asp Glu Leu Met 640
 625 630 635
 Glu Ile Phe Arg Arg Cys Lys Ile Pro Asn Thr Val Glu Glu Ala Val 655
 645 650
 Arg Ile Ile Thr Gly Gly Ala Pro Glu Leu Ala Val Glu Gly Asn Gly 670
 660 665
 Pro Val Glu Ser Asn Ala Val Leu Thr Lys Ala Val Lys Arg Pro Asn 685
 675 680
 Glu Asp Ser Asp Glu Asp Glu Glu Lys Gly Ala Val Val Pro Pro Val 700
 690 695
 His Asp Ile Tyr Arg Ala Arg Gln Gln Lys Arg Ile Arg 715
 705 710
 <210> 191
 <211> 442
 <212> PRT
 <213> Homo sapiens
 <400> 191
 Met Ala Ser Val Val Leu Pro Ser Gly Ser Gln Cys Ala Ala Ala 15
 1 5 10
 Ala Ala Ala Pro Pro Gly Leu Arg Leu Arg Leu Leu Leu Leu 30
 20 25
 Phe Ser Ala Ala Ala Leu Ile Pro Thr Gly Asp Gly Gln Asn Leu Phe 45
 35 40

Thr Lys Asp Val Thr Val Ile Glu Gly Glu Val Ala Thr Ile Ser Cys 60
 50 55
 Gln Val Asn Lys Ser Asp Asp Ser Val Ile Gln Leu Leu Asn Pro Asn 80
 65 70 75
 Arg Gln Thr Ile Tyr Phe Arg Asp Phe Arg Pro Leu Lys Asp Ser Arg 95
 85 90
 Phe Gln Leu Leu Asn Phe Ser Ser Ser Glu Leu Lys Val Ser Leu Thr 110
 100 105
 Asn Val Ser Ile Ser Asp Glu Gly Arg Tyr Phe Cys Gln Leu Tyr Thr 125
 115 120
 Asp Pro Pro Gln Glu Ser Tyr Thr Thr Ile Thr Val Leu Val Pro Pro 140
 130 135 140
 Arg Asn Leu Met Ile Asp Ile Gln Arg Asp Thr Ala Val Glu Gly Glu 160
 145 150 155
 Glu Ile Glu Val Asn Cys Thr Ala Met Ala Ser Lys Pro Ala Thr Thr 175
 165 170
 Ile Arg Trp Phe Lys Gly Asn Thr Glu Leu Lys Gly Lys Ser Glu Val 190
 180 185
 Glu Glu Trp Ser Asp Met Tyr Thr Val Thr Ser Gln Leu Met Leu Lys 205
 195 200
 Val His Lys Glu Asp Asp Gly Val Pro Val Ile Cys Gln Val Glu His 220
 210 215
 Pro Ala Val Thr Gly Asn Leu Gln Thr Gln Arg Tyr Leu Glu Val Gln 240
 225 230 235
 Tyr Lys Pro Gln Val His Ile Gln Met Thr Tyr Pro Leu Gln Gly Leu 255
 245 250
 Thr Arg Glu Gly Asp Ala Leu Glu Leu Thr Cys Glu Ala Ile Gly Lys 270
 260 265
 Pro Gln Pro Val Met Val Thr Trp Val Arg Val Asp Asp Glu Met Pro 285
 275 280
 Gln His Ala Val Leu Ser Gly Pro Asn Leu Phe Ile Asn Asn Leu Asn 300
 290 295
 Lys Thr Asp Asn Gly Thr Tyr Arg Cys Glu Ala Ser Asn Ile Val Gly 320
 305 310 315
 Lys Ala His Ser Asp Tyr Met Leu Tyr Val Tyr Asp Pro Thr Thr 335
 325 330
 Ile Pro Pro Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr 350
 340 345
 Thr Ile Leu Thr Ile Ile Thr Asp Ser Arg Ala Gly Glu Gly Ser 365
 355 360
 Ile Arg Ala Val Asp His Ala Val Ile Gly Val Val Ala Val Val 380
 370 375

Val Phe Ala Met Leu Cys Leu Leu Ile Ile Leu Gly Arg Tyr Phe Ala
385 390 395 400
Arg His Lys Gly Thr Tyr Phe Thr His Glu Ala Lys Gly Ala Asp Asp
405 410 415
Ala Ala Asp Ala Asp Thr Ala Ile Ile Asn Ala Glu Gly Gly Gln Asn
420 425 430
Asn Ser Glu Glu Lys Lys Glu Tyr Phe Ile
435 440
<210> 192
<211> 288
<212> PRT
<213> Homo sapiens
<400> 192
Met Ala Ala Val Leu Leu Gln Arg Val Glu Arg Leu Ser Asn Arg Val Val
1 5 10 15
Arg Val Leu Gly Cys Asn Pro Gly Pro Met Thr Leu Gln Gly Thr Asn
20 25 30
Thr Tyr Leu Val Gly Thr Gly Pro Arg Arg Ile Leu Ile Asp Thr Gly
35 40 45
Glu Pro Ala Ile Pro Glu Tyr Ile Ser Cys Leu Lys Gln Ala Leu Thr
50 55 60
Glu Phe Asn Thr Ala Ile Gln Glu Ile Val Val Thr His Trp His Arg
65 70 75 80
Asp His Ser Gly Gly Ile Gly Asp Ile Cys Lys Ser Ile Asn Asn Asp
85 90 95
Thr Thr Tyr Cys Ile Lys Lys Leu Pro Arg Asn Pro Gln Arg Glu Glu
100 105 110
Ile Ile Gly Asn Gly Glu Gln Gln Tyr Val Tyr Leu Lys Asp Gly Asp
115 120 125
Val Ile Lys Thr Glu Gly Ala Thr Leu Arg Val Leu Tyr Thr Pro Gly
130 135 140
His Thr Asp Asp His Met Ala Leu Leu Leu Glu Glu Asn Ala Ile
145 150 155 160
Phe Ser Gly Asp Cys Ile Leu Gly Glu Gly Thr Thr Val Phe Glu Asp
165 170 175
Leu Tyr Asp Tyr Met Asn Ser Leu Lys Glu Leu Lys Ile Lys Ala
180 185 190
Asp Ile Ile Tyr Pro Gly His Gly Pro Val Ile His Asn Ala Glu Ala
195 200 205
Lys Ile Gln Gln Tyr Ile Ser His Arg Asn Ile Arg Glu Gln Gln Ile
210 215 220
Leu Thr Leu Phe Arg Glu Asn Phe Glu Lys Ser Phe Thr Val Met Glu

225 230 235 240
Leu Val Lys Ile Ile Tyr Lys Asn Thr Pro Glu Asn Leu His Glu Met
245 250 255
Ala Lys His Asn Leu Leu Leu His Leu Lys Lys Leu Glu Lys Glu Gly
260 265 270
Lys Ile Phe Ser Asn Thr Asp Pro Asp Lys Lys Trp Lys Ala His Leu
275 280 285
<210> 193
<211> 872
<212> PRT
<213> Homo sapiens
<400> 193
Met Ala Pro Gly Ala Ala Gln Glu Leu Gln Ala Lys Leu Ala Glu Ile
1 5 10 15
Gly Ala Pro Ile Gln Gly Asn Arg Glu Glu Leu Val Glu Arg Leu Gln
20 25 30
Ser Tyr Thr Arg Gln Thr Gly Ile Val Leu Asn Arg Pro Val Leu Arg
35 40 45
Gly Glu Asp Gly Asp Lys Ala Ala Pro Pro Met Ser Ala Gln Leu
50 55 60
Pro Gly Ile Pro Met Pro Pro Pro Leu Gly Leu Pro Pro Leu Gln
65 70 75 80
Pro Pro Pro Pro Pro Pro Pro Gly Leu Gly Leu Gly Phe
85 90 95
Pro Met Ala His Pro Asn Leu Gly Pro Pro Pro Pro Leu Arg Val
100 105 110
Gly Glu Pro Val Ala Leu Ser Glu Glu Glu Arg Leu Lys Leu Ala Gln
115 120 125
Gln Gln Ala Ala Leu Leu Met Gln Gln Glu Glu Arg Ala Lys Gln Gln
130 135 140
Gly Asp His Ser Leu Lys Glu His Glu Leu Leu Glu Gln Lys Arg
145 150 155 160
Ala Ala Val Leu Leu Glu Gln Glu Arg Gln Gln Ile Ala Lys Met
165 170 175
Gly Thr Pro Val Pro Arg Pro Pro Gln Asp Met Gly Gln Ile Gly Val
180 185 190
Arg Thr Pro Leu Gly Pro Arg Val Ala Ala Pro Val Gly Pro Val Gly
195 200 205
Pro Thr Pro Thr Val Leu Pro Met Gly Ala Pro Val Pro Arg Pro Arg
210 215 220
Gly Pro Pro Pro Gly Asp Glu Asn Arg Glu Met Asp Asp Pro
225 230 235 240

Ser Val Gly Pro Lys Ile Pro Gln Ala Leu Glu Lys Ile Leu Gln Leu 245 250 255
 Lys Glu Ser Arg Gln Glu Met Asn Ser Gln Gln Glu Glu Glu 260 265 270
 Met Glu Thr Asp Ala Arg Ser Ser Leu Gly Gln Ser Ala Ser Glu Thr 275 280 285
 Glu Glu Asp Thr Val Ser Val Ser Lys Lys Glu Lys Asn Arg Lys Arg 290 295 300
 Arg Asn Arg Lys Lys Lys Lys Pro Gln Arg Val Arg Gly Val Ser 305 310 315 320
 Ser Glu Ser Ser Gly Asp Arg Glu Lys Asp Ser Thr Arg Ser Arg Gly 325 330 335
 Ser Asp Ser Pro Ala Ala Asp Val Glu Ile Glu Tyr Val Thr Glu Glu 340 345 350
 Pro Glu Ile Tyr Glu Pro Asn Phe Ile Phe Phe Lys Arg Ile Phe Glu 355 360 365
 Ala Phe Lys Leu Thr Asp Asp Val Lys Lys Glu Lys Glu Lys Glu Pro 370 375 380
 Glu Lys Leu Asp Lys Leu Glu Asn Ser Ala Ala Pro Lys Lys Lys Gly 385 390 395 400
 Phe Glu Glu Glu His Lys Asp Ser Asp Asp Ser Ser Asp Asp Glu 405 410 415
 Gln Glu Lys Lys Pro Glu Ala Pro Lys Leu Ser Lys Lys Lys Leu Arg 420 425 430
 Arg Met Asn Arg Phe Thr Val Ala Glu Leu Lys Gln Leu Val Ala Arg 435 440 445
 Pro Asp Val Val Glu Met His Asp Val Thr Ala Gln Asp Pro Lys Leu 450 455 460
 Leu Val His Leu Lys Ala Thr Arg Asn Ser Val Pro Val Pro Arg His 465 470 475 480
 Trp Cys Phe Lys Arg Lys Tyr Leu Gln Gly Lys Arg Gly Ile Glu Lys 485 490 495
 Pro Pro Phe Glu Leu Pro Asp Phe Ile Lys Arg Thr Gly Ile Gln Glu 500 505 510
 Met Arg Glu Ala Leu Gln Glu Lys Glu Glu Gln Lys Thr Met Lys Ser 515 520 525
 Lys Met Arg Glu Lys Val Arg Pro Lys Met Gly Lys Ile Asp Ile Asp 530 535 540
 Tyr Gln Lys Leu His Asp Ala Phe Phe Lys Trp Gln Thr Lys Pro Lys 545 550 555 560
 Leu Thr Ile His Gly Asp Leu Tyr Tyr Glu Gly Lys Glu Phe Glu Thr 565 570 575

396

Arg Leu Lys Glu Lys Lys Pro Gly Asp Leu Ser Asp Glu Leu Arg Ile 580 585 590
 Ser Leu Gly Met Pro Val Gly Pro Asn Ala His Lys Val Pro Pro Pro 595 600 605
 Trp Leu Ile Ala Met Gln Arg Tyr Gly Pro Pro Pro Ser Tyr Pro Asn 610 615 620
 Leu Lys Ile Pro Gly Leu Asn Ser Pro Ile Pro Glu Ser Cys Ser Phe 625 630 635 640
 Gly Tyr His Ala Gly Gly Trp Gly Lys Pro Pro Val Asp Glu Thr Gly 645 650 655
 Lys Pro Leu Tyr Gly Asp Val Phe Gly Thr Asn Ala Ala Glu Phe Gln 660 665 670
 Thr Lys Thr Glu Glu Glu Ile Asp Arg Thr Pro Trp Gly Glu Leu 675 680 685
 Glu Pro Ser Asp Glu Glu Ser Ser Glu Glu Glu Glu Glu Ser 690 695 700
 Asp Glu Asp Lys Pro Asp Glu Thr Gly Phe Ile Thr Pro Ala Asp Ser 705 710 715 720
 Gly Leu Ile Thr Pro Gly Gly Phe Ser Ser Val Pro Ala Gly Met Glu 725 730 735
 Thr Pro Glu Leu Ile Glu Leu Arg Lys Lys Ile Glu Glu Ala Met 740 745 750
 Asp Gly Ser Glu Thr Pro Gln Leu Phe Thr Val Leu Pro Glu Lys Arg 755 760 765
 Thr Ala Thr Val Gly Gly Ala Met Met Gly Ser Thr His Ile Tyr Asp 770 775 780
 Met Ser Thr Val Met Ser Arg Lys Gly Pro Ala Pro Glu Leu Gln Gly 785 790 795 800
 Val Glu Val Ala Leu Ala Pro Glu Glu Leu Glu Leu Asp Pro Met Ala 805 810 815
 Met Thr Gln Lys Tyr Glu Glu His Val Arg Glu Gln Gln Ala Gln Val 820 825 830
 Glu Lys Glu Asp Phe Ser Asp Met Val Ala Glu His Ala Ala Lys Gln 835 840 845
 Lys Gln Lys Lys Arg Lys Ala Gln Pro Gln Asp Ser Arg Gly Gly Ser 850 855 860
 Lys Lys Tyr Lys Glu Phe Lys Phe 865 870

397

<210> 194
 <211> 507
 <212> PRT
 <213> Homo sapiens

<400> 194
 Met Gly Cys Trp Gly Arg Asn Arg Gly Arg Leu Leu Cys Met Leu Ala 15
 1 10
 Leu Thr Phe Met Phe Met Val Leu Glu Val Val Val Ser Arg Val Thr 30
 20 25
 Ser Ser Leu Ala Met Leu Ser Asp Ser Phe His Met Leu Ser Asp Val 45
 35 40
 Leu Ala Leu Val Val Ala Leu Val Ala Glu Arg Phe Ala Arg Thr 60
 50 55
 His Ala Thr Gln Lys Asn Thr Phe Gly Trp Ile Arg Ala Glu Val Met 80
 65 70 75
 Gly Ala Leu Val Asn Ala Ile Phe Leu Thr Gly Leu Cys Phe Ala Ile 95
 85 90
 Leu Leu Glu Ala Ile Glu Arg Phe Ile Glu Pro His Glu Met Gln Gln 110
 100 105
 Pro Leu Val Val Leu Gly Val Gly Val Ala Gly Leu Leu Val Asn Val 125
 115 120
 Leu Gly Leu Cys Leu Phe His His Ser Gly Phe Ser Gln Asp Ser 140
 130 135
 Gly His Gly His Ser His Gly Gly His Gly His Gly Leu Pro 160
 145 150 155
 Lys Gly Pro Arg Val Lys Ser Thr Arg Pro Gly Ser Ser Asp Ile Asn 175
 165 170
 Val Ala Pro Gly Glu Gln Gly Pro Asp Gln Glu Glu Thr Asn Thr Leu 190
 180 185
 Val Ala Asn Thr Ser Asn Ser Asn Gly Leu Lys Leu Asp Pro Ala Asp 205
 195 200
 Pro Glu Asn Pro Arg Ser Gly Asp Thr Val Glu Val Gln Val Asn Gly 220
 210 215
 Asn Leu Val Arg Glu Pro Asp His Met Glu Leu Glu Asp Arg Ala 240
 225 230 235
 Gly Gln Leu Asn Met Arg Gly Val Phe Leu His Val Leu Gly Asp Ala 255
 245 250
 Leu Gly Ser Val Ile Val Val Val Asn Ala Leu Val Phe Tyr Phe Ser 270
 260 265
 Trp Lys Gly Cys Ser Glu Gly Asp Phe Cys Val Asn Pro Cys Phe Pro 285
 275 280
 Asp Pro Cys Lys Ala Phe Val Glu Ile Ile Asn Ser Thr His Ala Ser 300
 290 295
 Val Tyr Glu Ala Gly Pro Cys Trp Val Leu Tyr Leu Asp Pro Thr Leu 320
 305 310 315

398

Cys Val Val Met Val Cys Ile Leu Leu Tyr Thr Tyr Pro Leu Leu 335
 325 330
 Lys Glu Ser Ala Leu Ile Leu Leu Gln Thr Val Pro Lys Gln Ile Asp 350
 340 345
 Ile Arg Asn Leu Ile Lys Glu Leu Arg Asn Val Glu Gly Val Glu Glu 365
 355 360
 Val His Glu Leu His Val Trp Gln Leu Ala Gly Ser Arg Ile Ile Ala 380
 370 375
 Thr Val His Ile Lys Cys Glu Asp Pro Thr Ser Tyr Met Glu Val Ala 400
 385 390 395
 Lys Thr Ile Lys Asp Val Phe His Asn His Gly Ile His Ala Thr Thr 415
 405 410
 Ile Gln Pro Glu Phe Ala Ser Val Gly Ser Lys Ser Ser Val Val Pro 430
 420 425
 Cys Glu Leu Ala Cys Arg Thr Gln Cys Ala Leu Lys Gln Cys Cys Gly 445
 435 440
 Thr Leu Pro Gln Ala Pro Ser Gly Lys Asp Ala Glu Lys Thr Pro Ala 460
 450 455
 Val Ser Ile Ser Cys Leu Glu Leu Ser Asn Asn Leu Glu Lys Lys Pro 480
 465 470 475
 Arg Arg Thr Lys Ala Glu Asn Ile Pro Ala Val Val Ile Glu Ile Lys 495
 485 490
 Asn Met Pro Asn Lys Gln Pro Glu Ser Ser Leu 505
 500
 <210> 195
 <211> 317
 <212> PRT
 <213> Homo sapiens
 <400> 195
 Met Thr Glu Gln Met Thr Leu Arg Gly Thr Leu Lys Gly His Asn Gly 15
 1 5 10
 Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro Asp Met Ile Leu 30
 20 25
 Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys Leu Thr Arg Asp 45
 35 40
 Glu Thr Asn Tyr Gly Ile Pro Gln Arg Ala Leu Arg Gly His Ser His 60
 50 55
 Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln Phe Ala Leu Ser 80
 65 70 75
 Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp Leu Thr Thr Gly Thr 95
 85 90
 Thr Thr Arg Arg Phe Val Gly His Thr Lys Asp Val Leu Ser Val Ala 110
 100 105

399

Phe Ser Ser Asp Asn Arg Gln Ile Val Ser Gly Ser Arg Asp Lys Thr
 115 120
 Ile Lys Leu Trp Asn Thr Leu Gly Val Cys Lys Tyr Thr Val Gln Asp
 110 135 140
 Glu Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser
 145 150 155 160
 Ser Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val
 165 170 175
 Trp Asn Leu Ala Asn Cys Lys Leu Lys Thr Asn His Ile Gly His Thr
 180 185 190
 Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser Leu Cys Ala
 195 200 205
 Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp Leu Asn Glu Gly
 210 215 220
 Lys His Leu Tyr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys
 225 230 235 240
 Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile
 245 250 255
 Lys Ile Trp Asp Leu Glu Gly Lys Ile Ile Val Asp Glu Leu Lys Gln
 260 265 270
 Glu Val Ile Ser Thr Ser Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser
 275 280 285
 Leu Ala Trp Ser Ala Asp Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp
 290 295 300
 Asn Leu Val Arg Val Trp Gln Val Thr Ile Gly Thr Arg
 305 310 315
 <210> 196
 <211> 662
 <212> PRT
 <213> Homo sapiens
 <400> 196
 Met Ser His Val Ala Val Glu Asn Ala Leu Gly Leu Asp Gln Gln Phe
 1 5 10 15
 Ala Gly Leu Asp Leu Asn Ser Ser Asp Asn Gln Ser Gly Gly Ser Thr
 20 25 30
 Ala Ser Lys Gly Arg Tyr Ile Pro Pro His Leu Arg Asn Arg Glu Ala
 35 40 45
 Thr Lys Gly Phe Tyr Asp Lys Asp Ser Ser Gly Trp Ser Ser Ser Lys
 50 55 60
 Asp Lys Asp Ala Tyr Ser Ser Phe Gly Ser Arg Ser Asp Ser Arg Gly
 65 70 75 80
 Lys Ser Ser Phe Phe Ser Asp Arg Gly Ser Gly Ser Arg Gly Arg Phe

400

Asp Asp Arg Gly Arg Ser Asp Tyr Asp Gly Ile Gly Ser Arg Gly Asp
 85 90 95
 100 105 110
 Arg Ser Gly Phe Gly Lys Phe Glu Arg Gly Gly Asn Ser Arg Trp Cys
 115 120 125
 Asp Lys Ser Asp Glu Asp Asp Trp Ser Lys Pro Leu Pro Pro Ser Glu
 130 135 140
 Arg Leu Glu Gln Glu Leu Phe Ser Gly Gly Asn Thr Gly Ile Asn Phe
 145 150 155 160
 Glu Lys Tyr Asp Asp Ile Pro Val Glu Ala Thr Gly Asn Asn Cys Pro
 165 170 175
 Pro His Ile Glu Ser Phe Ser Asp Val Glu Met Gly Glu Ile Ile Met
 180 185 190
 Gly Asn Ile Glu Leu Thr Arg Tyr Thr Arg Pro Thr Pro Val Gln Lys
 195 200 205
 His Ala Ile Pro Ile Ile Lys Glu Lys Arg Asp Leu Met Ala Cys Ala
 210 215 220
 Gln Thr Gly Ser Gly Lys Thr Ala Ala Phe Leu Leu Pro Ile Leu Ser
 225 230 235 240
 Gln Ile Tyr Ser Asp Gly Pro Gly Glu Ala Leu Arg Ala Met Lys Glu
 245 250 255
 Asn Gly Arg Tyr Gly Arg Arg Lys Gln Tyr Pro Ile Ser Leu Val Leu
 260 265 270
 Ala Pro Thr Arg Glu Leu Ala Val Gln Ile Tyr Glu Glu Ala Arg Lys
 275 280 285
 Phe Ser Tyr Arg Ser Arg Val Arg Pro Cys Val Val Tyr Gly Gly Ala
 290 295 300
 Asp Ile Gly Gln Gln Ile Arg Asp Leu Glu Arg Gly Cys His Leu Leu
 305 310 315
 Val Ala Thr Pro Gly Arg Leu Val Asp Met Met Glu Arg Gly Lys Ile
 320 325 330 335
 Gly Leu Asp Phe Cys Lys Tyr Leu Val Leu Asp Glu Ala Asp Arg Met
 340 345 350
 Leu Asp Met Gly Phe Glu Pro Gln Ile Arg Arg Ile Val Glu Gln Asp
 355 360 365
 Thr Met Pro Pro Lys Gly Val Arg His Thr Met Met Phe Ser Ala Thr
 370 375 380
 Phe Pro Lys Glu Ile Gln Met Leu Ala Arg Asp Phe Leu Asp Glu Tyr
 385 390 395 400
 Ile Phe Leu Ala Val Gly Arg Val Gly Ser Thr Ser Glu Asn Ile Thr
 405 410 415

401

Gln Lys Val Val Trp Val Glu Ser Asp Lys Arg Ser Phe Leu Leu 420 425 430
 Asp Leu Leu Asn Ala Thr Gly Lys Asp Ser Leu Thr Leu Val Phe Val 435 440 445
 Glu Thr Lys Lys Gly Ala Asp Ser Leu Glu Asp Phe Leu Tyr His Glu 450 455 460
 Gly Tyr Ala Cys Thr Ser Ile His Gly Asp Arg Ser Gln Arg Asp Arg 465 470 475 480
 Glu Glu Ala Leu His Gln Phe Arg Ser Gly Lys Ser Pro Ile Leu Val 485 490 495
 Ala Thr Ala Val Ala Ala Arg Gly Leu Asp Ile Ser Asn Val Lys His 500 505 510
 Val Ile Asn Phe Asp Leu Pro Ser Asp Ile Glu Glu Tyr Val His Arg 515 520 525
 Ile Gly Arg Thr Gly Arg Val Gly Asn Leu Gly Leu Ala Thr Ser Phe 530 535 540
 Phe Asn Glu Arg Asn Ile Asn Ile Thr Lys Asp Leu Leu Asp Leu Leu 545 550 555 560
 Val Glu Ala Lys Gln Glu Val Pro Ser Trp Leu Glu Asn Met Ala Tyr 565 570 575
 Glu His His Tyr Lys Gly Ser Ser Arg Gly Arg Ser Lys Ser Ser Arg 580 585 590
 Phe Ser Gly Gly Phe Gly Ala Arg Asp Tyr Arg Gln Ser Ser Gly Ala 595 600 605
 Ser Ser Ser Ser Phe Ser Ser Arg Ala Ser Ser Ser Arg Ser Gly 610 615 620
 Gly Gly Gly His Gly Ser Ser Arg Gly Phe Gly Gly Gly Tyr Tyr Gly 625 630 635 640
 Gly Phe Tyr Asn Ser Asp Gly Tyr Gly Gly Asn Tyr Asn Ser Gln Gly 645 650 655
 Val Asp Trp Trp Gly Asn 660

<210> 197
 <211> 660
 <212> PRT
 <213> Homo sapiens

<400> 197
 Met Ser His Val Val Lys Asn Asp Pro Glu Leu Asp Gln Gln Leu 1 5 10 15
 Ala Asn Leu Asp Leu Asn Ser Glu Lys Gln Ser Gly Gly Ala Ser Thr 20 25 30
 Ala Ser Lys Gly Arg Tyr Ile Pro Pro His Leu Arg Asn Lys Glu Ala 35 40 45

402

Ser Lys Gly Phe His Asp Lys Asp Ser Ser Gly Trp Ser Cys Ser Lys 50 55 60
 Asp Lys Asp Ala Tyr Ser Ser Phe Gly Ser Arg Asp Ser Arg Gly Lys 65 70 75 80
 Pro Gly Tyr Phe Ser Glu Arg Gly Ser Gly Ser Arg Gly Arg Phe Asp 85 90 95
 Asp Arg Gly Arg Ser Asp Tyr Asp Gly Ile Gly Asn Arg Glu Arg Pro 100 105 110
 Gly Phe Gly Arg Phe Glu Arg Ser Gly His Ser Arg Trp Cys Asp Lys 115 120 125
 Ser Val Glu Asp Asp Trp Ser Lys Pro Leu Pro Pro Ser Glu Arg Leu 130 135 140
 Glu Gln Glu Leu Phe Ser Gly Gly Asn Thr Gly Ile Asn Phe Glu Lys 145 150 155 160
 Tyr Asp Asp Ile Pro Val Glu Ala Thr Gly Ser Asn Cys Pro Pro His 165 170 175
 Ile Glu Asn Phe Ser Asp Ile Asp Met Gly Glu Ile Ile Met Gly Asn 180 185 190
 Ile Glu Leu Thr Arg Tyr Thr Arg Pro Thr Pro Val Gln Lys His Ala 195 200 205
 Ile Pro Ile Ile Lys Gly Lys Arg Asp Leu Val Ala Cys Ala Gln Thr 210 215 220
 Gly Ser Gly Lys Thr Ala Ala Phe Leu Leu Pro Ile Leu Ser Gln Ile 225 230 235 240
 Tyr Thr Asp Gly Pro Gly Glu Ala Leu Lys Ala Val Lys Glu Asn Gly 245 250 255
 Arg Tyr Gly Arg Arg Lys Gln Tyr Pro Ile Ser Leu Val Leu Ala Pro 260 265 270
 Thr Arg Glu Leu Ala Val Gln Ile Tyr Glu Glu Ala Arg Lys Phe Ser 275 280 285
 Tyr Arg Ser Arg Val Arg Pro Cys Val Val Tyr Gly Gly Ala Asp Ile 290 295 300
 Gly Gln Gln Ile Arg Asp Leu Glu Arg Gly Cys His Leu Leu Val Ala 305 310 315 320
 Thr Pro Gly Arg Leu Val Asp Met Met Glu Arg Gly Lys Ile Gly Leu 325 330 335
 Asp Phe Cys Lys Tyr Leu Val Leu Asp Glu Ala Asp Arg Met Leu Asp 340 345 350
 Met Gly Phe Glu Pro Gln Ile Arg Arg Ile Val Glu Gln Asp Thr Met 355 360 365
 Pro Pro Lys Gly Val Arg His Thr Met Met Phe Ser Ala Thr Phe Pro 370 375 380

403

370 375 380
 Lys Glu Ile Gln Met Leu Ala Arg Asp Phe Leu Asp Glu Tyr Ile Phe 385 390 395 400
 Leu Ala Val Gly Arg Val Gly Ser Thr Ser Glu Asn Ile Thr Gln Lys 405 410 415
 Val Val Trp Val Glu Asp Leu Asp Lys Arg Ser Phe Leu Leu Asp Ile 420 425 430
 Leu Gly Ala Thr Gly Ser Asp Ser Leu Thr Leu Val Phe Val Glu Thr 435 440 445
 Lys Lys Gly Ala Asp Ser Leu Glu Asp Phe Leu Tyr His Glu Gly Tyr 450 455 460
 Ala Cys Thr Ser Ile His Gly Asp Arg Ser Gln Arg Asp Arg Glu Glu 465 470 475 480
 Ala Leu His Gln Phe Arg Ser Gly Lys Ser Pro Ile Leu Val Ala Thr 485 490 495
 Ala Val Ala Ala Arg Gly Leu Asp Ile Ser Asn Val Arg His Val Ile 500 505 510
 Asn Phe Asp Leu Pro Ser Asp Ile Glu Glu Tyr Val His Arg Ile Gly 515 520 525
 Arg Thr Gly Arg Val Gly Asn Leu Gly Leu Ala Thr Ser Phe Phe Asn 530 535 540
 Glu Lys Asn Met Asn Ile Thr Lys Asp Leu Leu Asp Leu Val Glu 545 550 555 560
 Ala Lys Gln Glu Val Pro Ser Trp Leu Glu Asn Met Ala Tyr Glu His 565 570 575
 His Tyr Lys Gly Gly Ser Arg Gly Arg Ser Lys Ser Asn Arg Phe Ser 580 585 590
 Gly Gly Phe Gly Ala Arg Asp Tyr Arg Gln Ser Ser Gly Ser Ser 595 600 605
 Ser Gly Phe Gly Ala Ser Arg Gly Ser Ser Arg Ser Gly Gly Gly 610 615 620
 Gly Tyr Gly Asp Ser Arg Gly Phe Gly Gly Gly Tyr Tyr Gly Gly Phe 625 630 635 640
 Tyr Asn Ser Asp Gly Tyr Gly Gly Asn Tyr Asn Ser Gln Gly Val Asp 645 650 655
 Trp Trp Gly Asn 660
 <210> 198
 <211> 1087
 <212> PRT
 <213> Homo sapiens
 <400> 198

404

Met Ala Asp His Val Gln Ser Leu Ala Gln Leu Glu Asn Leu Cys Lys 1 5 10 15
 Gln Leu Tyr Glu Thr Thr Asp Thr Thr Arg Leu Gln Ala Glu Lys 20 25 30
 Ala Leu Val Glu Phe Thr Asn Ser Pro Asp Cys Leu Ser Lys Cys Gln 35 40 45
 Leu Leu Leu Glu Arg Gly Ser Ser Tyr Ser Gln Leu Leu Ala Ala 50 55 60
 Thr Cys Leu Thr Lys Leu Val Ser Arg Thr Asn Asn Pro Leu Pro Leu 65 70 75 80
 Glu Gln Arg Ile Asp Ile Arg Asn Tyr Val Leu Asn Tyr Leu Ala Thr 85 90 95
 Arg Pro Lys Leu Ala Thr Phe Val Thr Gln Ala Leu Ile Gln Leu Tyr 100 105 110
 Ala Arg Ile Thr Lys Leu Gly Trp Phe Asp Cys Gln Lys Asp Asp Tyr 115 120 125
 Val Phe Arg Asn Ala Ile Thr Asp Val Thr Arg Phe Leu Gln Asp Ser 130 135 140
 Val Glu Tyr Cys Ile Ile Gly Val Thr Ile Leu Ser Gln Leu Thr Asn 145 150 155 160
 Glu Ile Asn Gln Ala Asp Thr Thr His Pro Leu Thr Lys His Arg Lys 165 170 175
 Ile Ala Ser Ser Phe Arg Asp Ser Ser Leu Phe Asp Ile Phe Thr Leu 180 185 190
 Ser Cys Asn Leu Leu Lys Gln Ala Ser Gly Lys Asn Leu Asn Leu Asn 195 200 205
 Asp Glu Ser Gln His Gly Leu Leu Met Gln Leu Leu Lys Leu Thr His 210 215 220
 Asn Cys Leu Asn Phe Asp Phe Ile Gly Thr Ser Thr Asp Glu Ser Ser 225 230 235 240
 Asp Asp Leu Cys Thr Val Gln Ile Pro Thr Ser Trp Arg Ser Ala Phe 245 250 255
 Leu Asp Ser Ser Thr Leu Gln Leu Phe Phe Asp Leu Tyr His Ser Ile 260 265 270
 Pro Pro Ser Phe Ser Pro Leu Val Leu Ser Cys Leu Val Gln Ile Ala 275 280 285
 Ser Val Arg Arg Ser Leu Phe Asn Asn Ala Glu Arg Ala Lys Phe Leu 290 295 300
 Ser His Leu Val Asp Gly Val Lys Arg Ile Leu Glu Asn Pro Gln Ser 305 310 315 320
 Leu Ser Asp Pro Asn Asn Tyr His Glu Phe Cys Arg Leu Leu Ala Arg 325 330 335

405

Leu Lys Ser Asn Tyr Gln Leu Gly Glu Leu Val Lys Val Glu Asn Tyr 340 345 350
 Pro Glu Val Ile Arg Leu Ile Ala Asn Phe Thr Val Thr Ser Leu Gln 355 360 365
 His Trp Glu Phe Ala Pro Asn Ser Val His Tyr Leu Leu Ser Leu Trp 370 375 380
 Gln Arg Leu Ala Ala Ser Val Pro Tyr Val Lys Ala Thr Glu Pro His 385 390 395 400
 Met Leu Glu Thr Tyr Thr Pro Glu Val Thr Lys Ala Tyr Ile Thr Ser 405 410 415
 Arg Leu Glu Ser Val His Ile Leu Arg Asp Gly Leu Glu Asp Pro 420 425 430
 Leu Glu Asp Thr Gly Leu Val Gln Gln Leu Asp Gln Leu Ser Thr 435 440 445
 Ile Gly Arg Cys Glu Tyr Glu Lys Thr Cys Ala Leu Leu Val Gln Leu 450 455 460
 Phe Asp Gln Ser Ala Gln Ser Tyr Gln Glu Leu Leu Gln Ser Ala Ser 465 470 475 480
 Ala Ser Pro Met Asp Ile Ala Val Gln Glu Gly Arg Leu Thr Trp Leu 485 490 495
 Val Tyr Ile Ile Gly Ala Val Ile Gly Gly Arg Val Ser Phe Ala Ser 500 505 510
 Thr Asp Glu Gln Asp Ala Met Asp Gly Glu Leu Val Cys Arg Val Leu 515 520 525
 Gln Leu Met Asn Leu Thr Asp Ser Arg Leu Ala Gln Ala Gly Asn Glu 530 535 540
 Lys Leu Glu Leu Ala Met Leu Ser Phe Phe Glu Gln Phe Arg Lys Ile 545 550 555 560
 Tyr Ile Gly Asp Gln Val Gln Lys Ser Ser Lys Leu Tyr Arg Arg Leu 565 570 575
 Ser Glu Val Leu Gly Leu Asn Asp Glu Thr Met Val Leu Ser Val Phe 580 585 590
 Ile Gly Lys Ile Ile Thr Asn Leu Lys Tyr Trp Gly Arg Cys Glu Pro 595 600 605
 Ile Thr Ser Lys Thr Leu Gln Leu Leu Asn Asp Leu Ser Ile Gly Tyr 610 615 620
 Ser Ser Val Arg Lys Leu Val Lys Leu Ser Ala Val Gln Phe Met Leu 625 630 635 640
 Asn Asn His Thr Ser Glu His Phe Ser Phe Leu Gly Ile Asn Asn Gln 645 650 655
 Ser Asn Leu Thr Asp Met Arg Cys Arg Thr Thr Phe Tyr Thr Ala Leu 660 665 670

Gly Arg Leu Leu Met Val Asp Leu Gly Glu Asp Glu Asp Gln Tyr Glu 675 680 685
 Gln Phe Met Leu Pro Leu Thr Ala Ala Phe Glu Ala Val Ala Gln Met 690 695 700
 Phe Ser Thr Asn Ser Phe Asn Glu Gln Ala Lys Arg Thr Leu Val 705 710 715 720
 Gly Leu Val Arg Asp Leu Arg Gly Ile Ala Phe Ala Phe Asn Ala Lys 725 730 735
 Thr Ser Phe Met Met Leu Phe Glu Trp Ile Tyr Pro Ser Tyr Met Pro 740 745 750
 Ile Leu Gln Arg Ala Ile Glu Leu Trp Tyr His Asp Pro Ala Cys Thr 755 760 765
 Thr Pro Val Leu Lys Leu Met Ala Glu Leu Val His Asn Arg Ser Gln 770 775 780
 Arg Leu Gln Phe Asp Val Ser Ser Pro Asn Gly Ile Leu Leu Phe Arg 785 790 795 800
 Glu Thr Ser Lys Met Ile Thr Met Tyr Gly Asn Arg Ile Leu Thr Leu 805 810 815
 Gly Glu Val Pro Lys Asp Gln Val Tyr Ala Leu Lys Leu Lys Gly Ile 820 825 830
 Ser Ile Cys Phe Ser Met Leu Lys Ala Ala Leu Ser Gly Ser Tyr Val 835 840 845
 Asn Phe Gly Val Phe Arg Leu Tyr Gly Asp Asp Ala Leu Asp Asn Ala 850 855 860
 Leu Gln Thr Phe Ile Lys Leu Leu Leu Ser Ile Pro His Ser Asp Leu 865 870 875 880
 Leu Asp Tyr Pro Lys Leu Ser Gln Ser Tyr Tyr Ser Leu Leu Glu Val 885 890 895
 Leu Thr Gln Asp His Met Asn Phe Ile Ala Ser Leu Glu Pro His Val 900 905 910
 Ile Met Tyr Ile Leu Ser Ser Ile Ser Glu Gly Leu Thr Ala Leu Asp 915 920 925
 Thr Met Val Cys Thr Gly Cys Ser Cys Leu Asp His Ile Val Thr 930 935 940
 Tyr Leu Phe Lys Gln Leu Ser Arg Ser Thr Lys Lys Arg Thr Thr Pro 945 950 955 960
 Leu Asn Gln Glu Ser Asp Arg Phe Leu His Ile Met Gln Gln His Pro 965 970 975
 Glu Met Ile Gln Gln Met Leu Ser Thr Val Leu Asn Ile Ile Ile Phe 980 985 990

Glu Asp Cys Arg Asn Gln Trp Ser Met Ser Arg Pro Leu Leu Gly Leu 1005
 995
 Ile Leu Leu Asn Glu Lys Tyr Phe Ser Asp Leu Arg Asn Ser Ile 1020
 1010
 Val Asn Ser Gln Pro Pro Gln Lys Gln Gln Ala Met His Leu Cys 1035
 1025
 Phe Glu Asn Leu Met Glu Gly Ile Glu Arg Asn Leu Leu Thr Lys 1050
 1040
 Asn Arg Asp Arg Phe Thr Gln Asn Leu Ser Ala Phe Arg Arg Glu 1065
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 Val Asn Asp Ser Met Lys Asn Ser Thr Tyr Gly Val Asn Ser Asn 1080
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 Asp Met Met Ser 1085

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 <211> 1088
 <212> PRT
 <213> Homo sapiens

 <400> 199
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 His Leu Tyr Ile Gly Thr Asp Leu Thr Gln Arg Ile Glu Ala Glu Lys 30
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 Ala Leu Leu Glu Leu Ile Asp Ser Pro Glu Cys Leu Ser Lys Cys Gln 45
 35
 Leu Leu Leu Glu Gln Gly Thr Thr Ser Tyr Ala Gln Leu Leu Ala Ala 60
 50
 Thr Cys Leu Ser Lys Leu Val Ser Arg Val Ser Pro Leu Pro Val Glu 80
 65 70 75
 Gln Arg Met Asp Ile Arg Asn Tyr Ile Leu Asn Tyr Val Ala Ser Gln 95
 85
 Pro Lys Leu Ala Pro Phe Val Ile Gln Ala Leu Ile Gln Val Ile Ala 110
 100
 Lys Ile Thr Lys Leu Gly Trp Phe Glu Val Gln Lys Asp Gln Phe Val 125
 115
 Phe Arg Glu Ile Ile Ala Asp Val Lys Lys Phe Leu Gln Gly Thr Val 140
 130 135
 Glu His Cys Ile Ile Gly Val Ile Ile Leu Ser Glu Leu Thr Gln Glu 160
 145 150 155
 Met Asn Leu Val Asp Tyr Ser Arg Pro Ser Ala Lys His Arg Lys Ile 175
 165 170
 Ala Thr Ser Phe Arg Asp Thr Ser Leu Lys Asp Val Leu Val Leu Ala 190
 180 185

408

Cys Ser Leu Leu Lys Glu Val Phe Ala Lys Pro Leu Asn Leu Gln Asp 205
 195 200
 Gln Cys Gln Gln Asn Leu Val Met Gln Val Leu Lys Leu Val Leu Asn 220
 210 215
 Cys Leu Asn Phe Asp Phe Ile Gly Ser Ser Ala Asp Glu Ser Ala Asp 240
 225 230 235
 Asp Leu Cys Thr Val Gln Ile Pro Thr Thr Trp Arg Thr Ile Phe Leu 255
 245 250
 Glu Pro Glu Thr Leu Asp Leu Phe Phe Asn Leu Tyr His Ser Leu Pro 270
 260 265
 Pro Leu Leu Ser Gln Leu Ala Leu Ser Cys Leu Val Gln Phe Ala Ser 285
 275 280
 Thr Arg Arg Ser Leu Phe Asn Ser Pro Glu Arg Ala Lys Tyr Leu Gly 300
 290 295
 Asn Leu Ile Lys Gly Val Lys Arg Ile Leu Glu Asn Pro Gln Gly Leu 320
 305 310 315
 Ser Asp Pro Gly Asn Tyr His Glu Phe Cys Arg Phe Leu Ala Arg Leu 335
 325 330
 Lys Thr Asn Tyr Gln Leu Gly Glu Leu Val Met Val Lys Glu Tyr Pro 350
 340 345
 Glu Val Ile Arg Leu Ile Ala Asn Phe Thr Ile Thr Ser Leu Gln His 365
 355 360
 Trp Glu Phe Ala Pro Asn Ser Val His Tyr Leu Leu Thr Leu Trp Gln 380
 370 375
 Arg Met Val Ala Ser Val Pro Phe Val Lys Ser Thr Glu Pro His Leu 400
 385 390 395
 Leu Asp Thr Tyr Ala Pro Glu Ile Thr Lys Ala Phe Ile Thr Ser Arg 415
 405 410
 Leu Asp Ser Val Ala Ile Val Val Arg Asp His Leu Asp Asp Pro Leu 430
 420 425
 Asp Asp Thr Ala Thr Val Phe Gln Gln Leu Glu Gln Leu Cys Thr Val 445
 435 440
 Ser Arg Cys Glu Tyr Glu Lys Thr Cys Ala Leu Leu Val Gln Leu Phe 460
 450 455
 Asp Gln Asn Ala Gln Asn Tyr Gln Lys Leu Leu His Pro Tyr Ser Gly 480
 465 470 475
 Val Thr Val Asp Ile Thr Ile Gln Glu Gly Arg Leu Ala Trp Leu Val 495
 485
 Tyr Leu Val Gly Thr Val Val Gly Gly Arg Leu Thr Tyr Thr Ser Thr 510
 500 505
 Asp Glu His Asp Ala Met Asp Gly Glu Leu Ser Cys Arg Val Phe Gln

409

515 520 525
 Leu Ile Ser Leu Met Asp Thr Gly Leu Pro Arg Cys Asn Glu Lys
 530 535 540
 Ile Glu Leu Ala Ile Leu Trp Phe Leu Asp Gln Phe Arg Lys Thr Tyr
 545 550 555 560
 Val Gly Asp Gln Leu Gln Arg Thr Ser Lys Val Tyr Ala Arg Met Ser
 565 570 575
 Glu Val Leu Gly Ile Thr Asp Asp Asn His Val Leu Glu Thr Phe Met
 580 585 590
 Thr Lys Ile Val Thr Asn Leu Lys Tyr Trp Gly Arg Tyr Glu Pro Val
 595 600 605
 Ile Ser Arg Thr Leu Gln Phe Leu Asn Asp Leu Ser Val Gly Tyr Ile
 610 615 620
 Leu Leu Lys Lys Leu Val Lys Ile Asp Ala Val Lys Phe Met Leu Lys
 625 630 635 640
 Asn His Thr Ser Glu His Phe Pro Phe Leu Gly Ile Ser Asp Asn His
 645 650 655
 Ser Leu Ser Asp Phe Arg Cys Arg Thr Thr Phe Tyr Thr Ala Leu Thr
 660 665 670
 Arg Leu Leu Met Val Asp Leu Gly Glu Asp Glu Asp Glu Phe Glu Asn
 675 680 685
 Phe Met Leu Pro Leu Thr Val Ala Phe Glu Thr Val Leu Gln Ile Phe
 690 695 700
 Asn Asn Asn Phe Lys Gln Glu Asp Val Lys Arg Met Leu Ile Gly Leu
 705 710 715 720
 Ala Arg Asp Leu Arg Gly Ile Ala Phe Ala Leu Asn Thr Lys Thr Ser
 725 730 735
 Tyr Thr Met Leu Phe Asp Trp Met Tyr Pro Thr Tyr Leu Pro Leu Leu
 740 745 750
 Gln Asn Ala Val Glu Arg Trp Tyr Gly Glu Pro Thr Cys Thr Thr Pro
 755 760 765
 Ile Leu Lys Leu Met Ala Glu Leu Met Gln Asn Arg Ser Gln Arg Leu
 770 775 780
 Asn Phe Asp Val Ser Ser Pro Asn Gly Ile Leu Leu Phe Arg Glu Ala
 785 790 795 800
 Ser Lys Met Val Cys Thr Tyr Gly Asn Gln Ile Leu Ser Leu Gly Ser
 805 810 815
 Leu Ser Lys Asp Gln Ile Tyr Pro Met Lys Leu Lys Gly Ile Ser Ile
 820 825 830
 Cys Tyr Ser Ala Leu Lys Ser Ala Leu Cys Gly Asn Tyr Val Ser Phe
 835 840 845

410

Gly Val Phe Lys Leu Tyr Gly Asp Asn His Phe Asp Asn Val Leu Gln
 850 855 860
 Ala Phe Val Lys Met Leu Leu Ser Val Ser His Ser Asp Leu Leu Gln
 865 870 875 880
 Tyr Arg Lys Leu Ser Gln Ser Tyr Tyr Pro Leu Leu Glu Cys Leu Thr
 885 890 895
 Gln Asp His Met Ser Phe Ile Ile Asn Leu Glu Pro Pro Val Leu Met
 900 905 910
 Tyr Val Leu Thr Ser Ile Ser Glu Gly Leu Thr Thr Leu Asp Thr Val
 915 920 925
 Val Ser Ser Ser Cys Cys Thr Ser Leu Asp Tyr Ile Val Thr Tyr Leu
 930 935 940
 Phe Lys His Ile Ala Lys Glu Gly Lys Lys Pro Tyr Arg Cys Arg Glu
 945 950 955 960
 Ala Thr Gln Ala Gly Gln Arg Leu Leu His Phe Met Gln Gln Asn Pro
 965 970 975
 Asp Val Leu Gln Gln Met Ser Val Leu Met Asn Thr Ile Val Phe
 980 985 990
 Glu Asp Cys Arg Asn Gln Trp Ser Val Ser Arg Pro Leu Leu Gly Leu
 995 1000 1005
 Ile Leu Leu Asn Glu Lys Tyr Phe Ser Glu Leu Arg Ala Ser Leu
 1010 1015 1020
 Ile Asn Ser Gln Pro Leu Pro Lys Gln Glu Val Leu Ala Gln Cys
 1025 1030 1035
 Phe Arg Asn Leu Met Glu Gly Val Glu Gln Asn Leu Ser Val Lys
 1040 1045 1050
 Asn Arg Asp Arg Phe Thr Gln Asn Leu Ser Val Phe Arg Arg Asp
 1055 1060 1065
 Val Ala Glu Ala Leu Arg Ser Asp Gly Asn Thr Glu Pro Cys Ser
 1070 1075 1080
 Leu Asp Met Met Ser
 1085
 <210> 200
 <211> 1154
 <212> PRT
 <213> Homo sapiens
 <400> 200
 Met Ser Ser Asn Ile His Ala Asn His Leu Ser Leu Asp Ala Ser Ser
 1 5 10 15
 Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
 20 25 30
 Ser Ser Ser Ser Val His Glu Pro Lys Met Asp Ala Leu Ile Ile Pro
 35 40 45

411

Val Thr Met Glu Val Pro Cys Asp Ser Arg Gly Gln Arg Met Trp Trp
50 55 60
Ala Phe Leu Ala Ser Ser Met Val Thr Phe Phe Gly Gly Leu Phe Ile
65 70 75 80
Ile Leu Leu Trp Arg Thr Leu Lys Tyr Leu Trp Thr Val Cys Cys His
85 90 95
Cys Gly Gly Lys Thr Lys Glu Ala Gln Lys Ile Asn Asn Gly Ser Ser
100 105 110
Gln Ala Asp Gly Thr Leu Lys Pro Val Asp Glu Lys Glu Glu Ala Val
115 120 125
Ala Ala Glu Val Gly Trp Met Thr Ser Val Lys Asp Trp Ala Gly Val
130 135 140
Met Ile Ser Ala Gln Thr Leu Thr Gly Arg Val Leu Val Val Leu Val
145 150 155 160
Phe Ala Leu Ser Ile Gly Ala Leu Val Ile Tyr Phe Ile Asp Ser Ser
165 170 175
Asn Pro Ile Glu Ser Cys Gln Asn Phe Tyr Lys Asp Phe Thr Leu Gln
180 185 190
Ile Asp Met Ala Phe Asn Val Phe Phe Leu Leu Tyr Phe Gly Leu Arg
195 200 205
Phe Ile Ala Ala Asn Asp Lys Leu Trp Phe Trp Leu Glu Val Asn Ser
210 215 220
Val Val Asp Phe Phe Thr Val Pro Pro Val Phe Val Ser Val Tyr Leu
225 230 235 240
Asn Arg Ser Trp Leu Gly Leu Arg Phe Leu Arg Ala Leu Arg Leu Ile
245 250 255
Gln Phe Ser Glu Ile Leu Gln Phe Leu Asn Ile Leu Lys Thr Ser Asn
260 265 270
Ser Ile Lys Leu Val Asn Leu Leu Ser Ile Phe Ile Ser Thr Trp Leu
275 280 285
Thr Ala Ala Gly Phe Ile His Leu Val Glu Asn Ser Gly Asp Pro Trp
290 295 300
Glu Asn Phe Gln Asn Asn Gln Ala Leu Thr Tyr Trp Glu Cys Val Tyr
305 310 315 320
Leu Leu Met Val Thr Met Ser Thr Val Gly Tyr Gly Asp Val Tyr Ala
325 330 335
Lys Thr Thr Leu Gly Arg Leu Phe Met Val Phe Phe Ile Leu Gly Gly
340 345 350
Leu Ala Met Phe Ala Ser Tyr Val Pro Glu Ile Ile Glu Leu Ile Gly
355 360 365
Asn Arg Lys Lys Tyr Gly Gly Ser Tyr Ser Ala Val Ser Gly Arg Lys

370 375 380
His Ile Val Val Cys Gly His Ile Thr Leu Glu Ser Val Ser Asn Phe
385 390 395 400
Leu Lys Asp Phe Leu His Lys Asp Arg Asp Asp Val Asn Val Glu Ile
405 410 415
Val Phe Leu His Asn Ile Ser Pro Asn Leu Glu Leu Glu Ala Leu Phe
420 425 430
Lys Arg His Phe Thr Gln Val Glu Phe Tyr Gln Gly Ser Val Leu Asn
435 440 445
Pro His Asp Leu Ala Arg Val Lys Ile Glu Ser Ala Asp Ala Cys Leu
450 455 460
Ile Leu Ala Asn Lys Tyr Cys Ala Asp Pro Asp Ala Glu Asp Ala Ser
465 470 475 480
Asn Ile Met Arg Val Ile Ser Ile Lys Asn Tyr His Pro Lys Ile Arg
485 490 495
Ile Ile Thr Gln Met Leu Gln Tyr His Asn Lys Ala His Leu Leu Asn
500 505 510
Ile Pro Ser Trp Asn Trp Lys Glu Gly Asp Asp Ala Ile Cys Leu Ala
515 520 525
Glu Leu Lys Leu Gly Phe Ile Ala Gln Ser Cys Leu Ala Gln Gly Leu
530 535 540
Ser Thr Met Leu Ala Asn Leu Phe Ser Met Arg Ser Phe Ile Lys Ile
545 550 555 560
Glu Glu Asp Thr Trp Gln Lys Tyr Tyr Leu Glu Gly Val Ser Asn Glu
565 570 575
Met Tyr Thr Glu Tyr Leu Ser Ser Ala Phe Val Gly Leu Ser Phe Pro
580 585 590
Thr Val Cys Glu Leu Cys Phe Val Lys Leu Lys Leu Leu Met Ile Ala
595 600 605
Ile Glu Tyr Lys Ser Ala Asn Arg Glu Ser Arg Ile Leu Ile Asn Pro
610 615 620
Gly Asn His Leu Lys Ile Gln Glu Gly Thr Leu Gly Phe Phe Ile Ala
625 630 635 640
Ser Asp Ala Lys Glu Val Lys Arg Ala Phe Phe Tyr Cys Lys Ala Cys
645 650 655
His Asp Asp Ile Thr Asp Pro Lys Arg Ile Lys Lys Cys Gly Cys Lys
660 665 670
Arg Leu Glu Asp Glu Gln Pro Ser Thr Leu Ser Pro Lys Lys Gln
675 680 685
Arg Asn Gly Gly Met Arg Asn Ser Pro Asn Thr Ser Pro Lys Leu Met
690 695 700

Arg His Asp Pro Leu Leu Ile Pro Gly Asn Asp Gln Ile Asp Asn Met
705 710 715 720

Asp Ser His Val Lys Lys Tyr Asp Ser Thr Gly Met Phe His Trp Cys
725 730 735

Ala Pro Lys Glu Ile Glu Lys Val Ile Leu Thr Arg Ser Glu Ala Ala
740 745 750

Met Thr Val Leu Ser Gly His Val Val Cys Ile Phe Gly Asp Val
755 760 765

Ser Ser Ala Leu Ile Gly Leu Arg Asn Leu Val Met Pro Leu Arg Ala
770 775 780

Ser Asn Phe His Tyr His Glu Leu Lys His Ile Val Phe Val Gly Ser
785 790 795 800

Ile Glu Tyr Leu Lys Arg Glu Trp Glu Thr Leu His Asn Phe Pro Lys
805 810 815

Val Ser Ile Leu Pro Gly Thr Pro Leu Ser Arg Ala Asp Leu Arg Ala
820 825 830

Val Asn Ile Asn Leu Cys Asp Met Cys Val Ile Leu Ser Ala Asn Gln
835 840 845

Asn Asn Ile Asp Asp Thr Ser Leu Gln Asp Lys Glu Cys Ile Leu Ala
850 855 860

Ser Leu Asn Ile Lys Ser Met Gln Phe Asp Asp Ser Ile Gly Val Leu
865 870 875 880

Gln Ala Asn Ser Gln Gly Phe Thr Pro Gly Met Asp Arg Ser Ser
885 890 895

Pro Asp Asn Ser Pro Val His Gly Met Leu Arg Gln Pro Ser Ile Thr
900 905 910

Thr Gly Val Asn Ile Pro Ile Ile Thr Glu Leu Val Asn Asp Thr Asn
915 920 925

Val Gln Phe Leu Asp Gln Asp Asp Asp Asp Pro Asp Thr Glu Leu
930 935 940

Tyr Leu Thr Gln Pro Phe Ala Cys Gly Thr Ala Phe Ala Val Ser Val
945 950 955 960

Leu Asp Ser Leu Met Ser Ala Thr Tyr Phe Asn Asp Asn Ile Leu Thr
965 970 975

Leu Ile Arg Thr Leu Val Thr Gly Gly Ala Thr Pro Glu Leu Glu Ala
980 985 990

Leu Ile Ala Glu Glu Asn Ala Leu Arg Gly Gly Tyr Ser Thr Pro Gln
995 1000 1005

Thr Leu Ala Asn Arg Asp Arg Cys Arg Val Ala Gln Leu Ala Leu
1010 1015 1020

Leu Asp Gly Pro Phe Ala Asp Leu Gly Asp Gly Cys Tyr Gly
1025 1030 1035

Asp Leu Phe Cys Lys Ala Leu Lys Thr Tyr Asn Met Leu Cys Phe
1040 1045 1050

Gly Ile Tyr Arg Leu Arg Asp Ala His Leu Ser Thr Pro Ser Gln
1055 1060 1065

Cys Thr Lys Arg Tyr Val Ile Thr Asn Pro Pro Tyr Glu Phe Glu
1070 1075 1080

Leu Val Pro Thr Asp Leu Ile Phe Cys Leu Met Gln Phe Asp His
1085 1090 1095

Asn Ala Gly Gln Ser Arg Ala Ser Leu Ser His Ser Ser His Ser
1100 1105 1110

Ser Gln Ser Ser Ser Lys Lys Ser Ser Ser Val His Ser Ile Pro
1115 1120 1125

Ser Thr Ala Asn Arg Gln Asn Arg Pro Lys Ser Arg Glu Ser Arg
1130 1135 1140

Asp Lys Gln Lys Tyr Val Gln Glu Glu Arg Leu
1145 1150

<210> 201
<211> 2552
<212> PRT
<213> Homo sapiens

<400> 201
Val Asp Pro Asp Leu Gly Glu Asn Gly Thr Leu Val Tyr Ser Ile Gln
1 5 10 15

Pro Pro Asn Lys Phe Tyr Ser Leu Asn Ser Thr Thr Gly Lys Ile Arg
20 25 30

Thr Thr His Ala Met Leu Asp Arg Glu Asn Pro Asp Pro His Glu Ala
35 40 45

Glu Leu Met Arg Lys Ile Val Val Ser Val Thr Asp Cys Gly Arg Pro
50 55 60

Pro Leu Lys Ala Thr Ser Ser Ala Thr Val Phe Val Asn Leu Leu Asp
65 70 75 80

Leu Asn Asp Asn Asp Pro Thr Phe Gln Asn Leu Pro Phe Val Ala Glu
85 90 95

Val Leu Glu Gly Ile Pro Ala Gly Val Ser Ile Tyr Gln Val Val Ala
100 105 110

Ile Asp Leu Asp Glu Gly Leu Asn Gly Leu Val Ser Tyr Arg Met Pro
115 120 125

Val Gly Met Pro Arg Met Asp Phe Leu Ile Asn Ser Ser Ser Gly Val
130 135 140

Val Val Thr Thr Thr Glu Leu Asp Arg Glu Arg Ile Ala Glu Tyr Gln
145 150 155 160

Leu Arg Val Val Ala Ser Asp Ala Gly Thr Pro Thr Lys Ser Ser Thr

165 170 175
 Ser Thr Leu Thr Ile His Leu Leu Asp Val Asn Asp Glu Thr Pro Thr 190
 180
 Phe Phe Pro Ala Val Tyr Asn Val Ser Val Ser Glu Asp Val Pro Arg 205
 195
 Glu Phe Arg Val Val Trp Leu Asn Cys Thr Asp Asn Asp Val Gly Leu 220
 210 215
 Asn Ala Glu Leu Ser Tyr Phe Ile Thr Gly Gly Asn Val Asp Gly Lys 240
 225 230 235
 Phe Ser Val Gly Tyr Arg Asp Ala Val Val Arg Thr Val Val Gly Leu 255
 245
 Asp Arg Glu Thr Thr Ala Ala Tyr Met Leu Ile Leu Glu Ala Ile Asp 270
 260 265
 Asn Gly Pro Val Gly Lys Arg His Thr Gly Thr Ala Thr Val Phe Val 285
 275 280
 Thr Val Leu Asp Val Asn Asp Asn Arg Pro Ile Phe Leu Gln Ser Ser 300
 290 295
 Tyr Glu Ala Ser Val Pro Glu Asp Ile Pro Glu Gly His Ser Ile Leu 320
 305 310 315
 Gln Leu Lys Ala Thr Asp Ala Asp Glu Gly Glu Phe Gly Arg Val Trp 335
 325 330
 Tyr Arg Ile Leu His Gly Asn His Gly Asn Asn Phe Arg Ile His Val 350
 340 345
 Ser Asn Gly Leu Leu Met Arg Gly Pro Arg Pro Leu Asp Arg Glu Arg 365
 355 360
 Asn Ser Ser His Val Leu Ile Val Glu Ala Tyr Asn His Asp Leu Gly 380
 370 375
 Pro Met Arg Ser Ser Val Arg Val Ile Val Tyr Val Glu Asp Ile Asn 400
 385 390 395
 Asp Glu Ala Pro Val Phe Thr Gln Gln Tyr Ser Arg Leu Gly Leu 415
 405 410
 Arg Glu Thr Ala Gly Ile Gly Thr Ser Val Ile Val Val Gln Ala Thr 430
 420 425
 Asp Arg Asp Ser Gly Asp Gly Gly Leu Val Asn Tyr Arg Ile Leu Ser 445
 435 440
 Gly Ala Glu Gly Lys Phe Glu Ile Asp Glu Ser Thr Gly Leu Ile Ile 460
 450 455
 Thr Val Asn Tyr Leu Asp Tyr Glu Thr Lys Thr Ser Tyr Met Met Asn 480
 465 470 475
 Val Ser Ala Thr Asp Gln Ala Pro Pro Phe Asn Gln Gly Phe Cys Ser 495
 485 490

Val Tyr Ile Thr Leu Leu Asn Glu Leu Asp Glu Ala Val Gln Phe Ser 510
 500 505
 Asn Ala Ser Tyr Glu Ala Ala Ile Leu Glu Asn Leu Ala Leu Gly Thr 525
 515 520
 Glu Ile Val Arg Val Gln Ala Tyr Ser Ile Asp Asn Leu Asn Gln Ile 540
 530 535
 Thr Tyr Arg Phe Asp Ala Tyr Thr Ser Thr Gln Ala Lys Ala Leu Phe 560
 545 550 555
 Lys Ile Asp Ala Ile Thr Gly Val Ile Thr Val Gln Gly Leu Val Asp 575
 565 570
 Arg Glu Lys Gly Asp Phe Tyr Thr Leu Thr Val Val Ala Asp Asp Gly 590
 580 585
 Gly Pro Lys Val Asp Ser Thr Val Val Tyr Ile Thr Val Leu Asp 605
 595 600
 Glu Asn Asp Asn Ser Pro Arg Phe Asp Phe Thr Ser Asp Ser Ala Val 620
 610 615
 Ser Ile Pro Glu Asp Cys Pro Val Gly Gln Arg Val Ala Thr Val Lys 640
 625 630 635
 Ala Trp Asp Pro Asp Ala Gly Ser Asn Gly Gln Val Val Phe Ser Leu 655
 645 650
 Ala Ser Gly Asn Ile Ala Gly Ala Phe Glu Ile Val Thr Thr Asn Asp 670
 660 665
 Ser Ile Gly Glu Val Phe Val Ala Arg Pro Leu Asp Arg Glu Glu Leu 685
 675 680
 Asp His Tyr Ile Leu Gln Val Val Ala Ser Asp Arg Gly Thr Pro Pro 700
 690 695
 Arg Lys Lys Asp His Ile Leu Gln Val Thr Ile Leu Asp Ile Asn Asp 720
 705 710 715
 Asn Pro Pro Val Ile Glu Ser Pro Phe Gly Tyr Asn Val Ser Val Asn 735
 725 730
 Glu Asn Val Gly Gly Gly Thr Ala Val Val Gln Val Arg Ala Thr Asp 750
 740 745
 Arg Asp Ile Gly Ile Asn Ser Val Leu Ser Tyr Tyr Ile Thr Glu Gly 765
 755 760
 Asn Lys Asp Met Thr Phe Arg Met Asp Arg Ile Ser Gly Glu Ile Ala 780
 770 775
 Thr Arg Pro Ala Pro Asp Arg Glu Arg Gln Ser Phe Tyr His Leu 800
 785 790 795
 Val Ala Thr Val Glu Asp Glu Gly Thr Pro Thr Leu Ser Ala Thr Thr 815
 805 810
 His Val Tyr Val Thr Ile Val Asp Glu Asn Asp Asn Ala Pro Met Phe 830
 820 825

Gln Gln Pro His Tyr Glu Val Leu Leu Asp Glu Gly Pro Asp Thr Leu 835 840 845
 Asn Thr Ser Leu Ile Thr Ile Gln Ala Leu Asp Leu Asp Glu Gly Pro 850 855 860 865
 Asn Gly Thr Val Thr Tyr Ala Ile Val Ala Gly Asn Ile Val Asn Thr 870 875 880 885
 Phe Arg Ile Asp Arg His Met Gly Val Ile Thr Ala Ala Lys Glu Leu 890 895
 Asp Tyr Glu Ile Ser His Gly Arg Tyr Thr Leu Ile Val Thr Ala Thr 900 905 910
 Asp Gln Cys Pro Ile Leu Ser His Arg Leu Thr Ser Thr Thr Thr Val 915 920 925
 Leu Val Asn Val Asn Asp Ile Asn Asp Asn Val Pro Thr Phe Pro Arg 930 935 940
 Asp Tyr Glu Gly Pro Phe Glu Val Thr Glu Gly Gln Pro Gly Pro Arg 945 950 955 960
 Val Trp Thr Phe Leu Ala His Asp Arg Asp Ser Gly Pro Asn Gly Gln 965 970 975
 Val Glu Tyr Ser Ile Met Asp Gly Asp Pro Leu Gly Glu Phe Val Ile 980 985 990
 Ser Pro Val Glu Gly Val Leu Arg Val Arg Lys Asp Val Glu Leu Asp 995 1000 1005
 Arg Glu Thr Ile Ala Phe Tyr Asn Leu Thr Ile Cys Ala Arg Asp 1010 1015 1020
 Arg Gly Met Pro Pro Leu Ser Ser Thr Met Leu Val Gly Ile Arg 1025 1030 1035
 Val Leu Asp Ile Asn Asp Asn Asp Pro Val Leu Leu Asn Leu Pro 1040 1045 1050
 Met Asn Ile Thr Ile Ser Glu Asn Ser Pro Val Ser Ser Phe Val 1055 1060 1065
 Ala His Val Leu Ala Ser Asp Ala Asp Ser Gly Cys Asn Ala Arg 1070 1075 1080
 Leu Thr Phe Asn Ile Thr Ala Gly Asn Arg Glu Arg Ala Phe Phe 1085 1090 1095
 Ile Asn Ala Thr Thr Gly Ile Val Thr Val Asn Arg Pro Leu Asp 1100 1105 1110
 Arg Glu Arg Ile Pro Glu Tyr Lys Leu Thr Ile Ser Val Lys Asp 1115 1120 1125
 Asn Pro Glu Asn Pro Arg Ile Ala Arg Arg Asp Tyr Asp Leu Leu 1130 1135 1140
 Leu Ile Phe Leu Ser Asp Glu Asn Asp Asn His Pro Leu Phe Thr 1145 1150 1155

Lys Ser Thr Tyr Gln Ala Glu Val Met Glu Asn Ser Pro Ala Gly 1160 1165 1170
 Thr Pro Leu Thr Val Leu Asn Gly Pro Ile Leu Ala Leu Asp Ala 1175 1180 1185
 Asp Gln Asp Ile Tyr Ala Val Val Thr Tyr Gln Leu Leu Gly Ala 1190 1195 1200
 Gln Ser Gly Leu Phe Asp Ile Asn Ser Ser Thr Gly Val Val Thr 1205 1210 1215
 Val Arg Ser Gly Val Ile Ile Asp Arg Glu Ala Phe Ser Pro Pro 1220 1225 1230
 Ile Leu Glu Leu Leu Leu Ala Glu Asp Ile Gly Leu Leu Asn 1235 1240 1245
 Ser Thr Ala His Leu Leu Ile Thr Ile Leu Asp Asp Asn Asp Asn 1250 1255 1260
 Arg Pro Thr Phe Ser Pro Ala Thr Leu Thr Val His Leu Leu Glu 1265 1270 1275
 Asn Cys Pro Pro Gly Phe Ser Val Leu Gln Val Thr Ala Thr Asp 1280 1285 1290
 Glu Asp Ser Gly Leu Asn Gly Glu Leu Val Tyr Arg Ile Glu Ala 1295 1300 1305
 Gly Ala Gln Asp Arg Phe Leu Ile His Leu Val Thr Gly Val Ile 1310 1315 1320
 Arg Val Gly Asn Ala Thr Ile Asp Arg Glu Glu Gln Glu Ser Tyr 1325 1330 1335
 Arg Leu Thr Val Val Ala Thr Asp Arg Gly Thr Val Pro Leu Ser 1340 1345 1350
 Gly Thr Ala Ile Val Thr Ile Leu Ile Asp Asp Ile Asn Asp Ser 1355 1360 1365
 Arg Pro Glu Phe Leu Asn Pro Ile Gln Thr Val Ser Val Leu Glu 1370 1375 1380
 Ser Ala Glu Pro Gly Thr Val Ile Ala Asn Ile Thr Ala Ile Asp 1385 1390 1395
 His Asp Leu Asn Pro Lys Leu Glu Tyr His Ile Val Gly Ile Val 1400 1405 1410
 Ala Lys Asp Asp Thr Asp Arg Leu Val Pro Asn Gln Glu Asp Ala 1415 1420 1425
 Phe Ala Val Asn Ile Asn Thr Gly Ser Val Met Val Lys Ser Pro 1430 1435 1440
 Met Asn Arg Glu Leu Val Ala Thr Tyr Glu Val Thr Leu Ser Val 1445 1450 1455

Ile Asp Asn Ala Ser Asp Leu Pro Glu Arg Ser Val Ser Val Pro 1460 1465 1470
 Asn Ala Lys Leu Thr Val Asn Val Leu Asp Val Asn Asp Asn Thr 1475 1480 1485
 Pro Gln Phe Lys Pro Phe Gly Ile Thr Tyr Tyr Met Glu Arg Ile 1490 1495 1500
 Leu Glu Gly Ala Thr Pro Gly Thr Thr Leu Ile Ala Val Ala Ala 1505 1510 1515
 Val Asp Pro Asp Lys Gly Leu Asn Gly Leu Val Thr Tyr Thr Leu 1520 1525 1530
 Leu Asp Leu Val Pro Pro Gly Tyr Val Gln Leu Glu Asp Ser Ser 1535 1540 1545
 Ala Gly Lys Val Ile Ala Asn Arg Thr Val Asp Tyr Glu Glu Val 1550 1555 1560
 His Trp Leu Asn Phe Thr Val Arg Ala Ser Asp Asn Gly Ser Pro 1565 1570 1575
 Pro Arg Ala Ala Glu Ile Pro Val Tyr Leu Glu Ile Val Asp Ile 1580 1585 1590
 Asn Asp Asn Asn Pro Ile Phe Asp Gln Pro Ser Tyr Gln Glu Ala 1595 1600 1605
 Val Phe Glu Asp Val Pro Val Gly Thr Ile Ile Leu Thr Val Thr 1610 1615 1620
 Ala Thr Asp Ala Asp Ser Gly Asn Phe Ala Leu Ile Glu Tyr Ser 1625 1630 1635
 Leu Gly Asp Gly Glu Ser Lys Phe Ala Ile Asn Pro Thr Thr Gly 1640 1645 1650
 Asp Ile Tyr Val Leu Ser Ser Leu Asp Arg Glu Lys Lys Asp His 1655 1660 1665
 Tyr Ile Leu Thr Ala Leu Ala Lys Asp Asn Pro Gly Asp Val Ala 1670 1675 1680
 Ser Asn Arg Arg Glu Asn Ser Val Gln Val Val Ile Gln Val Leu 1685 1690 1695
 Asp Val Asn Asp Cys Arg Pro Gln Phe Ser Lys Pro Gln Phe Ser 1700 1705 1710
 Thr Ser Val Tyr Glu Asn Glu Pro Ala Gly Thr Ser Val Ile Thr 1715 1720 1725
 Met Met Ala Thr Asp Gln Asp Glu Gly Pro Asn Gly Glu Leu Thr 1730 1735 1740
 Tyr Ser Leu Glu Gly Pro Gly Val Glu Ala Phe His Val Asp Met 1745 1750 1755
 Asp Ser Gly Leu Val Thr Thr Gln Arg Pro Leu Gln Ser Tyr Glu 1760 1765 1770

Lys Phe Ser Leu Thr Val Val Ala Thr Asp Gly Gly Glu Pro Pro 1775 1780 1785
 Leu Trp Gly Thr Thr Met Leu Leu Val Glu Val Ile Asp Val Asn 1790 1795 1800
 Asp Asn Arg Pro Val Phe Val Arg Pro Pro Asn Gly Thr Ile Leu 1805 1810 1815
 His Ile Arg Glu Glu Ile Pro Leu Arg Ser Asn Val Tyr Glu Val 1820 1825 1830
 Tyr Ala Thr Asp Lys Asp Glu Gly Leu Asn Gly Ala Val Arg Tyr 1835 1840 1845
 Ser Phe Leu Lys Thr Ala Gly Asn Arg Asp Trp Glu Phe Phe Ile 1850 1855 1860
 Ile Asp Pro Ile Ser Gly Leu Ile Gln Thr Ala Gln Arg Leu Asp 1865 1870 1875
 Arg Glu Ser Gln Ala Val Tyr Ser Leu Ile Leu Val Ala Ser Asp 1880 1885 1890
 Leu Gly Gln Pro Val Pro Tyr Glu Thr Met Gln Pro Leu Gln Val 1895 1900 1905
 Ala Leu Glu Asp Ile Asp Asp Asn Glu Pro Leu Phe Val Arg Pro 1910 1915 1920
 Pro Lys Gly Ser Pro Gln Tyr Gln Leu Leu Thr Val Pro Glu His 1925 1930 1935
 Ser Pro Arg Gly Thr Leu Val Gly Asn Val Thr Gly Ala Val Asp 1940 1945 1950
 Ala Asp Glu Gly Pro Asn Ala Ile Val Tyr Tyr Phe Ile Ala Ala 1955 1960 1965
 Gly Asn Glu Glu Lys Asn Phe His Leu Gln Pro Asp Gly Cys Leu 1970 1975 1980
 Leu Val Leu Arg Asp Leu Asp Arg Glu Arg Glu Ala Ile Phe Ser 1985 1990 1995
 Phe Ile Val Lys Ala Ser Ser Asn Arg Ser Trp Thr Pro Pro Arg 2000 2005 2010
 Gly Pro Ser Pro Thr Leu Asp Leu Val Ala Asp Leu Thr Leu Gln 2015 2020 2025
 Glu Val Arg Val Val Leu Glu Asp Ile Asn Asp Gln Pro Pro Arg 2030 2035 2040
 Phe Thr Lys Ala Glu Tyr Thr Ala Gly Val Ala Thr Asp Ala Lys 2045 2050 2055
 Val Gly Ser Glu Leu Ile Gln Val Leu Ala Leu Asp Ala Asp Ile 2060 2065 2070
 Gly Asn Asn Ser Leu Val Phe Tyr Ser Ile Leu Ala Ile His Tyr

2075 2080 2085
 Phe Arg Ala Leu Ala Asn Asp Ser Glu Asp Val Gly Gln Val Phe
 2090 2095
 Thr Met Gly Ser Met Asp Gly Ile Leu Arg Thr Phe Asp Leu Phe
 2105 2110 2115
 Met Ala Tyr Ser Pro Gly Tyr Phe Val Val Asp Ile Val Ala Arg
 2120 2125 2130
 Asp Leu Ala Gly His Asn Asp Thr Ala Ile Ile Gly Ile Tyr Ile
 2135 2140 2145
 Leu Arg Asp Asp Gln Arg Val Lys Ile Val Ile Asn Glu Ile Pro
 2150 2155 2160
 Asp Arg Val Arg Gly Phe Glu Glu Glu Phe Ile His Leu Leu Ser
 2165 2170 2175
 Asn Ile Thr Gly Ala Ile Val Asn Thr Asp Asn Val Gln Phe His
 2180 2185 2190
 Val Asp Lys Lys Gly Arg Val Asn Phe Ala Gln Thr Glu Leu Leu
 2195 2200 2205
 Ile His Val Val Asn Arg Asp Thr Asn Arg Ile Leu Asp Val Asp
 2210 2215 2220
 Arg Val Ile Gln Met Ile Asp Glu Asn Lys Glu Gln Leu Arg Asn
 2225 2230 2235
 Leu Phe Arg Asn Tyr Asn Val Leu Asp Val Gln Pro Ala Ile Ser
 2240 2245 2250
 Val Arg Leu Pro Asp Asp Met Ser Ala Leu Gln Met Ala Ile Ile
 2255 2260 2265
 Val Leu Ala Ile Leu Leu Phe Leu Ala Ala Met Leu Phe Val Leu
 2270 2275 2280
 Met Asn Trp Tyr Tyr Arg Thr Val His Lys Arg Lys Leu Lys Ala
 2285 2290 2295
 Ile Val Ala Gly Ser Ala Gly Asn Arg Gly Phe Ile Asp Ile Met
 2300 2305 2310
 Asp Met Pro Asn Thr Asn Lys Tyr Ser Phe Asp Gly Ala Asn Pro
 2315 2320 2325
 Val Trp Leu Asp Pro Phe Cys Arg Asn Leu Glu Leu Ala Ala Gln
 2330 2335 2340
 Ala Glu His Glu Asp Asp Leu Pro Glu Asn Leu Ser Glu Ile Ala
 2345 2350 2355
 Asp Leu Trp Asn Ser Pro Thr Arg Thr His Gly Thr Phe Gly Arg
 2360 2365 2370
 Glu Pro Ala Ala Val Lys Pro Asp Asp Asp Arg Tyr Leu Arg Ala
 2375 2380 2385

Ala Ile Gln Glu Tyr Asp Asn Ile Ala Lys Leu Gly Gln Ile Ile
 2190 2195 2400
 Arg Glu Gly Pro Ile Lys Gly Ser Leu Leu Lys Val Val Leu Glu
 2405 2410 2415
 Asp Tyr Leu Arg Leu Lys Lys Leu Phe Ala Gln Arg Met Val Gln
 2420 2425 2430
 Lys Ala Ser Ser Cys His Ser Ser Ile Ser Glu Leu Ile Gln Thr
 2435 2440 2445
 Glu Leu Asp Glu Glu Pro Gly Asp His Ser Pro Gly Gln Gly Ser
 2450 2455 2460
 Leu Arg Phe Arg His Lys Pro Pro Val Glu Leu Lys Gly Pro Asp
 2465 2470 2475
 Gly Ile His Val Val His Gly Ser Thr Gly Thr Leu Leu Ala Thr
 2480 2485 2490
 Asp Leu Asn Ser Leu Pro Glu Glu Asp Gln Lys Gly Leu Gly Arg
 2495 2500 2505
 Ser Leu Glu Thr Leu Thr Ala Ala Glu Ala Thr Ala Phe Glu Arg
 2510 2515 2520
 Asn Ala Arg Thr Glu Ser Ala Lys Ser Thr Pro Leu His Lys Leu
 2525 2530 2535
 Arg Asp Val Ile Met Glu Thr Pro Leu Glu Ile Thr Glu Leu
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 Met Arg Asp Tyr Asp Glu Val Thr Ala Phe Leu Gly Glu Trp Gly Pro
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 Gly Phe Thr Gly Leu Ser Ser Val Phe Leu Ile Ala Thr Pro Glu His
 35 40 45
 Arg Cys Arg Val Pro Asp Ala Ala Asn Leu Ser Ser Ala Trp Arg Asn
 50 55 60
 His Thr Val Pro Leu Arg Leu Arg Asp Gly Arg Glu Val Pro His Ser
 65 70 75 80
 Cys Arg Arg Tyr Arg Leu Ala Thr Ile Ala Asn Phe Ser Ala Leu Gly
 85 90 95
 Leu Glu Pro Gly Arg Asp Val Asp Leu Gly Gln Leu Glu Gln Ser
 100 105 110
 Cys Leu Asp Gly Trp Glu Phe Ser Gln Asp Val Tyr Leu Ser Thr Ile
 115 120 125

Val Thr Glu Trp Asn Leu Val Cys Glu Asp Trp Lys Ala Pro Leu 130 140
 Thr Ile Ser Leu Phe Phe Val Gly Val Leu Leu Gly Ser Phe Ile Ser 145 150 155 160
 Gly Gln Leu Ser Asp Arg Phe Gly Arg Lys Asn Val Leu Phe Val Thr 165 170 175
 Met Gly Met Gln Thr Gly Phe Ser Phe Leu Gln Ile Phe Ser Lys Asn 180 185 190
 Phe Glu Met Phe Val Val Leu Phe Val Leu Val Gly Met Gly Gln Ile 195 200 205
 Ser Asn Tyr Val Ala Ala Phe Val Leu Gly Thr Glu Ile Leu Gly Lys 210 215 220
 Ser Val Arg Ile Ile Phe Ser Thr Leu Gly Val Cys Ile Phe Tyr Ala 225 230 235 240
 Phe Gly Tyr Met Val Leu Pro Leu Phe Ala Tyr Phe Ile Arg Asp Trp 245 250 255
 Arg Met Leu Leu Val Ala Leu Thr Met Pro Gly Val Leu Cys Val Ala 260 265 270
 Leu Trp Trp Phe Ile Pro Glu Ser Pro Arg Trp Leu Ile Ser Gln Gly 275 280 285
 Arg Phe Glu Glu Ala Glu Val Ile Ile Arg Lys Ala Ala Lys Ala Asn 290 295 300
 Gly Ile Val Val Pro Ser Thr Ile Phe Asp Pro Ser Glu Leu Gln Asp 305 310 315 320
 Leu Ser Ser Lys Lys Gln Gln Ser His Asn Ile Leu Asp Leu Leu Arg 325 330 335
 Thr Trp Asn Ile Arg Met Val Thr Ile Met Ser Ile Met Leu Trp Met 340 345 350
 Thr Ile Ser Val Gly Tyr Phe Gly Leu Ser Leu Asp Thr Pro Asn Leu 355 360 365
 His Gly Asp Ile Phe Val Asn Cys Phe Leu Ser Ala Met Val Glu Val 370 375 380
 Pro Ala Tyr Val Leu Ala Trp Leu Leu Gln Tyr Leu Pro Arg Arg 385 390 395 400
 Tyr Ser Met Ala Thr Ala Leu Phe Leu Gly Gly Ser Val Leu Leu Phe 405 410 415
 Met Gln Leu Val Pro Pro Asp Leu Tyr Tyr Leu Ala Thr Val Leu Val 420 425 430
 Met Val Gly Lys Phe Gly Val Thr Ala Ala Phe Ser Met Val Tyr Val 435 440 445
 Tyr Thr Ala Glu Leu Tyr Pro Thr Val Val Arg Asn Met Gly Val Gly 450 455 460

424

450 455 460
 Val Ser Ser Thr Ala Ser Arg Leu Gly Ser Ile Leu Ser Pro Tyr Phe 465 470 475 480
 Val Tyr Leu Gly Ala Tyr Asp Arg Phe Leu Pro Tyr Ile Leu Met Gly 485 490 495
 Ser Leu Thr Ile Leu Thr Ala Ile Leu Thr Leu Phe Leu Pro Glu Ser 500 505 510
 Phe Gly Thr Pro Leu Pro Asp Thr Ile Asp Gln Met Leu Arg Val Lys 515 520 525
 Gly Met Lys His Arg Lys Thr Pro Ser His Thr Arg Met Leu Lys Asp 530 535 540
 Gly Gln Glu Arg Pro Thr Ile Leu Lys Ser Thr Ala Phe 545 550 555
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 Glu Asn Phe Val Gln Ala Ser Thr Cys Lys Gly Thr Leu Gln Ala Phe 20 25 30
 Asn Ile Leu Thr Arg His Leu Asp Leu Asp Pro Leu Asp His Arg Asn 35 40 45
 Phe Tyr Ser Lys Leu Lys Ser Lys Val Thr Thr Trp Lys Ala Lys Ala 50 55 60
 Leu Trp Tyr Lys Leu Asp Lys Arg Gly Ser His Lys Glu Tyr Lys Arg 65 70 75 80
 Gly Lys Ser Cys Thr Asn Thr Lys Cys Leu Ile Val Gly Gly Gly Pro 85 90 95
 Cys Gly Leu Arg Thr Ala Ile Glu Leu Ala Tyr Leu Gly Ala Lys Val 100 105 110 115
 Val Val Val Glu Lys Arg Asp Ser Phe Ser Arg Asn Asn Val Leu His 115 120 125
 Leu Trp Pro Phe Thr Ile His Asp Leu Arg Gly Leu Gly Ala Lys Lys 130 135 140 145
 Phe Tyr Gly Lys Phe Cys Ala Gly Ser Ile Asp His Ile Ser Ile Arg 145 150 155 160
 Gln Leu Gln Leu Ile Leu Phe Lys Val Ala Leu Met Leu Gly Val Glu 165 170 175
 Ile His Val Asn Val Glu Phe Val Lys Val Leu Glu Pro Pro Glu Asp 180 185 190 195

425

Gln Glu Asn Gln Lys Ile Gly Trp Arg Ala Glu Phe Leu Pro Thr Asp 195 200
His Ser Leu Ser Glu Phe Glu Phe Asp Val Ile Ile Gly Ala Asp Gly 210 220
Arg Arg Asn Thr Leu Glu Gly Phe Arg Arg Lys Glu Phe Arg Gly Lys 225 230 235 240
Leu Ala Ile Ala Ile Thr Ala Asn Phe Ile Asn Arg Asn Ser Thr Ala 245 250 255
Glu Ala Lys Val Glu Glu Ile Ser Gly Val Ala Phe Ile Phe Asn Gln 260 265 270
Lys Phe Gln Asn Asp Leu Lys Glu Glu Thr Gly Ile Asp Leu Glu Asn 275 280 285
Ile Val Tyr Tyr Lys Asp Cys Thr His Tyr Phe Val Met Thr Ala Lys 290 295 300
Lys Gln Ser Leu Leu Asp Lys Gly Val Ile Ile Asn Asp Tyr Ile Asp 305 310 315 320
Thr Glu Met Leu Leu Cys Ala Glu Asn Val Asn Gln Asp Asn Leu Leu 325 330 335
Ser Tyr Ala Arg Glu Ala Ala Asp Phe Ala Thr Asn Tyr Gln Leu Pro 340 345 350
Ser Leu Asp Phe Ala Met Asn His Tyr Gly Gln Pro Asp Val Ala Met 355 360 365
Phe Asp Phe Thr Cys Met Tyr Ala Ser Glu Asn Ala Ala Leu Val Arg 370 375 380
Glu Arg Gln Ala His Gln Leu Leu Val Ala Leu Val Gly Asp Ser Leu 385 390 395 400
Leu Glu Pro Phe Trp Pro Met Gly Thr Gly Cys Ala Arg Gly Phe Leu 405 410 415
Ala Ala Phe Asp Thr Ala Trp Met Val Lys Ser Trp Asn Gln Gly Thr 420 425 430
Pro Pro Leu Glu Leu Leu Ala Glu Arg Glu Ser Leu Tyr Arg Leu Leu 435 440 445
Pro Gln Thr Thr Pro Glu Asn Ile Asn Lys Asn Phe Glu Gln Tyr Thr 450 455 460
Leu Asp Pro Gly Thr Arg Tyr Pro Asn Leu Asn Ser His Cys Val Arg 465 470 475 480
Pro His Gln Val Lys His Leu Tyr Ile Thr Lys Glu Leu Glu His Tyr 485 490 495
Pro Leu Glu Arg Leu Gly Ser Val Arg Arg Ser Val Asn Leu Ser Arg 500 505 510
Lys Glu Ser Asp Ile Arg Pro Ser Lys Leu Leu Thr Trp Cys Gln Gln 515 520 525

426

Gln Thr Glu Gly Tyr Gln His Val Asn Val Thr Asp Leu Thr Thr Ser 530 535 540
Trp Arg Ser Gly Leu Ala Leu Cys Ala Ile Ile His Arg Phe Arg Pro 545 550 555 560
Glu Leu Ile Asn Phe Asp Ser Leu Asn Glu Asp Asp Ala Val Glu Asn 565 570 575
Asn Gln Leu Ala Phe Asp Val Ala Glu Arg Glu Phe Gly Ile Pro Pro 580 585 590
Val Thr Thr Gly Lys Glu Met Ala Ser Ala Gln Glu Pro Asp Lys Leu 595 600 605
Ser Met Val Met Tyr Leu Ser Lys Phe Tyr Glu Leu Phe Arg Gly Thr 610 615 620 625
Pro Leu Arg Pro Val Asp Ser Trp Arg Lys Asn Tyr Gly Glu Asn Ala 630 635 640
Asp Leu Ser Leu Ala Lys Ser Ser Ile Ser Asn Asn Tyr Leu Asn Leu 645 650 655
Thr Phe Pro Arg Lys Arg Thr Pro Arg Val Asp Gly Gln Thr Gly Glu 660 665 670
Asn Asp Met Asn Lys Arg Arg Arg Lys Gly Phe Thr Asn Leu Asp Glu 675 680 685
Pro Ser Asn Phe Ser Ser Arg Ser Leu Gly Ser Asn Gln Glu Cys Gly 690 695 700
Ser Ser Lys Glu Gly Gly Asn Gln Asn Lys Val Lys Ser Met Ala Asn 705 710 715 720
Gln Leu Leu Ala Lys Phe Glu Glu Ser Thr Arg Asn Pro Ser Leu Met 725 730 735
Lys Gln Glu Arg Arg Val Ser Gly Ile Gly Lys Pro Val Leu Cys Ser 740 745 750
Ser Ser Gly Pro Pro Val His Ser Cys Cys Pro Lys Pro Glu Glu Ala 755 760 765
Thr Pro Ser Pro Ser Pro Pro Leu Lys Arg Gln Phe Pro Ser Val Val 770 775 780
Val Thr Gly His Val Leu Arg Glu Leu Lys Gln Val Ser Ala Gly Ser 785 790 795 800
Glu Cys Leu Ser Arg Pro Trp Arg Ala Arg Ala Lys Ser Asp Leu Gln 805 810 815
Leu Gly Gly Thr Glu Asn Phe Ala Thr Leu Pro Ser Thr Arg Pro Arg 820 825 830
Ala Gln Ala Leu Ser Gly Val Leu Trp Arg Leu Gln Gln Val Glu Glu 835 840 845
Lys Ile Leu Gln Lys Arg Ala Gln Asn Leu Ala Asn Arg Glu Phe His 850 855 860

427

850 855 860
 Thr Lys Asn Ile Lys Glu Lys Ala His Leu Ala Ser Met Phe Gly 880
 865 870 875
 His Gly Asp Phe Pro Gln Asn Lys Leu Leu Ser Lys Gly Leu Ser His 895
 885 890
 Thr His Pro Pro Ser Pro Ser Arg Leu Pro Ser Pro Asp Pro Ala 910
 900 905
 Ala Ser Ser Ser Pro Ser Thr Val Asp Ser Ala Ser Pro Ala Arg Lys 925
 915 920
 Glu Lys Lys Ser Pro Ser Gly Phe His Phe His Pro Ser His Leu Arg 940
 930 935
 Thr Val His Pro Gln Leu Thr Val Gly Lys Val Ser Ser Gly Ile Gly 960
 945 950 955
 Ala Ala Ala Glu Val Leu Val Asn Leu Tyr Met Asn Asp His Arg Pro 975
 965 970
 Lys Ala Gln Ala Thr Ser Pro Asp Leu Glu Ser Met Arg Lys Ser Phe 990
 980 985
 Pro Leu Asn Leu Gly Gly Ser Asp Thr Cys Tyr Phe Cys Lys Lys Arg 1005
 995 1000
 Val Tyr Val Met Glu Arg Leu Ser Ala Glu Gly His Phe His 1020
 1010 1015
 Arg Glu Cys Phe Arg Cys Ser Ile Cys Ala Thr Thr Leu Arg Leu 1035
 1025 1030
 Ala Ala Tyr Thr Phe Asp Cys Asp Glu Gly Lys Phe Tyr Cys Lys 1050
 1040 1045
 Pro His Phe Ile His Cys Lys Thr Asn Ser Lys Gln Arg Lys Arg 1065
 1055 1060
 Arg Ala Glu Leu Lys Gln Gln Arg Glu Glu Glu Ala Thr Trp Gln 1080
 1070 1075
 Glu Gln Glu Ala Pro Arg Arg Asp Thr Pro Thr Glu Ser Ser Cys 1095
 1085 1090
 Ala Val Ala Ala Ile Gly Thr Leu Glu Gly Ser Pro Pro Val His 1110
 1100 1105
 Phe Ser Leu Pro Val Leu His Pro Leu Leu Gly 1120
 1115 1120
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 <213> Homo sapiens
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 Ile Cys Asp Gln Ile Ser Asp Ala Val Leu Asp Ala His Leu Lys Gln 45
 35 40
 Asp Pro Asn Ala Lys Val Ala Cys Glu Thr Val Cys Lys Thr Gly Met 60
 50 55
 Val Leu Leu Cys Gly Glu Ile Thr Ser Met Ala Met Val Asp Tyr Gln 80
 65 70 75
 Arg Val Val Arg Asp Thr Ile Lys His Ile Gly Tyr Asp Ser Ala 95
 85 90
 Lys Gly Phe Asp Phe Lys Thr Cys Asn Val Leu Val Ala Leu Glu Gln 110
 100 105
 Gln Ser Pro Asp Ile Ala Gln Cys Val His Leu Asp Arg Asn Glu Glu 125
 115 120
 Asp Val Gly Ala Gly Asp Gln Gly Leu Met Phe Gly Tyr Ala Thr Asp 140
 130 135
 Glu Thr Glu Glu Cys Met Pro Leu Thr Ile Ile Leu Ala His Lys Leu 160
 145 150 155
 Asn Ala Arg Met Ala Asp Leu Arg Arg Ser Gly Leu Leu Pro Trp Leu 175
 165 170
 Arg Pro Asp Ser Lys Thr Gln Val Thr Val Gln Tyr Met Gln Asp Asn 190
 180 185
 Gly Ala Val Ile Pro Val Arg Ile His Thr Ile Val Ile Ser Val Gln 205
 195 200
 His Asn Glu Asp Ile Thr Leu Glu Glu Met Arg Arg Ala Leu Lys Glu 220
 210 215
 Gln Val Ile Arg Ala Val Val Pro Ala Lys Tyr Leu Asp Glu Asp Thr 240
 225 230 235
 Val Tyr His Leu Gln Pro Ser Gly Arg Phe Val Ile Gly Gly Pro Gln 255
 245 250
 Gly Asp Ala Gly Val Thr Gly Arg Lys Ile Ile Val Asp Thr Tyr Gly 270
 260 265
 Gly Trp Gly Ala His Gly Gly Ala Phe Ser Gly Lys Asp Tyr Thr 285
 275 280
 Lys Val Asp Arg Ser Ala Tyr Ala Ala Arg Trp Val Ala Lys Ser 300
 290 295
 Leu Val Lys Ala Gly Leu Cys Arg Arg Val Leu Val Gln Val Ser Tyr 320
 305 310 315
 Ala Ile Gly Val Ala Glu Pro Leu Ser Ile Ser Ile Phe Thr Tyr Gly 335
 325 330
 Thr Ser Gln Lys Thr Glu Arg Glu Leu Leu Asp Val Val His Lys Asn 350
 340 345

Phe Asp Leu Arg Pro Gly Val Ile Val Arg Asp Leu Asp Leu Lys Lys
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 385 390 395
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 Ala Tyr Pro Phe Asn Ala Lys Gln Pro Thr Asp Met Ala Arg Arg Gln
 35 40 45
 Gln Lys Ile Ser Lys Gln Gln Leu Gln Thr Val Lys Asp Arg Phe Gln
 50 55 60
 Ala Phe Leu Asn Gly Glu Thr Gln Ile Met Ala Asp Glu Ala Phe Met
 65 70 75 80
 Asn Ala Val Gln Ser Tyr Tyr Glu Val Phe Leu Lys Ser Asp Arg Val
 85 90 95
 Ala Arg Met Val Gln Ser Gly Cys Ser Ala Asn Asp Ser Arg Glu
 100 105 110
 Val Phe Lys Lys His Ile Glu Lys Arg Val Arg Ser Leu Pro Glu Ile
 115 120 125
 Asp Gly Leu Ser Lys Glu Thr Val Leu Ser Ser Trp Met Ala Lys Phe
 130 135 140
 Asp Ala Ile Tyr Arg Gly Glu Glu Asp Pro Arg Lys Gln Gln Ala Arg
 145 150 155 160
 Met Thr Ala Ser Ala Ala Ser Glu Leu Ile Leu Ser Lys Glu Gln Leu
 165 170 175
 Tyr Glu Met Phe Gln Asn Ile Leu Gly Ile Lys Lys Phe Glu His Gln
 180 185 190
 Leu Leu Tyr Asn Ala Cys Gln Leu Asp Asn Pro Asp Glu Gln Ala Ala
 195 200 205
 Gln Ile Arg Arg Glu Leu Asp Gly Arg Leu Gln Met Ala Asp Gln Ile
 210 215 220
 Ala Arg Glu Arg Lys Phe Pro Lys Phe Val Ser Lys Glu Met Glu Asn
 225 230 235 240
 Met Tyr Ile Glu Glu Leu Lys Ser Ser Val Asn Leu Leu Met Ala Asn

430

245 250 255
 Leu Glu Ser Met Pro Val Ser Lys Gly Gly Glu Phe Lys Leu Gln Lys
 260 265 270
 Leu Lys Arg Ser His Asn Ala Ser Ile Ile Asp Met Gly Glu Glu Ser
 275 280 285
 Glu Asn Gln Leu Ser Lys Ser Asp Val Val Leu Ser Phe Ser Leu Glu
 290 295 300
 Val Val Ile Met Glu Val Gln Gly Leu Lys Ser Leu Ala Pro Asn Arg
 305 310 315 320
 Ile Val Tyr Cys Thr Met Glu Val Glu Gly Gly Glu Lys Leu Gln Thr
 325 330 335
 Asp Gln Ala Glu Ala Ser Lys Pro Thr Trp Gly Thr Gln Gly Asp Phe
 340 345 350
 Ser Thr Thr His Ala Leu Pro Ala Val Lys Val Lys Leu Phe Thr Glu
 355 360 365
 Ser Thr Gly Val Leu Ala Leu Glu Asp Lys Glu Leu Gly Arg Val Ile
 370 375 380
 Leu His Pro Thr Pro Asn Ser Pro Lys Gln Ser Glu Trp His Lys Met
 385 390 395 400
 Thr Val Ser Lys Asn Cys Pro Asp Gln Asp Leu Lys Ile Lys Leu Ala
 405 410 415
 Val Arg Met Asp Lys Pro Gln Asn Met Lys His Ser Gly Tyr Leu Trp
 420 425 430
 Ala Ile Gly Lys Asn Val Trp Lys Arg Trp Lys Lys Arg Phe Phe Val
 435 440 445
 Leu Val Gln Val Ser Gln Tyr Thr Phe Ala Met Cys Ser Tyr Arg Glu
 450 455 460
 Lys Lys Ala Glu Pro Gln Glu Leu Leu Gln Leu Asp Gly Tyr Thr Val
 465 470 475 480
 Asp Tyr Thr Asp Pro Gln Pro Gly Leu Glu Gly Gly Arg Ala Phe Phe
 485 490 495
 Asn Ala Val Lys Glu Gly Asp Thr Val Ile Phe Ala Ser Asp Asp Glu
 500 505 510
 Gln Asp Arg Ile Leu Trp Val Gln Ala Met Tyr Arg Ala Thr Gly Gln
 515 520 525
 Ser His Lys Pro Val Pro Pro Thr Gln Val Gln Lys Leu Asn Ala Lys
 530 535 540
 Gly Gly Asn Val Pro Gln Leu Asp Ala Pro Ile Ser Gln Phe Ser Gly
 545 550 555 560
 Leu Lys Asp Ala Asp Arg Ala Gln Lys His Gly Met Asp Glu Phe Ile
 565 570 575

431

Ser Ser Asn Pro Cys Asn Phe Asp His Ala Ser Leu Phe Glu Met Val
580 585 590

Gln Arg Leu Thr Leu Asp His Arg Leu Asn Asp Ser Tyr Ser Cys Leu
595 600 605

Gly Trp Phe Ser Pro Gly Gln Val Phe Val Leu Asp Glu Tyr Cys Ala
610 615 620

Arg Asn Gly Val Arg Gly Cys His Arg His Leu Cys Tyr Leu Arg Asp
625 630 635 640

Leu Leu Glu Arg Ala Glu Asn Gly Ala Met Ile Asp Pro Thr Leu Leu
645 650 655

His Tyr Ser Phe Ala Phe Cys Ala Ser His Val His Gly Asn Arg Pro
660 665 670

Asp Gly Ile Gly Thr Val Thr Val Glu Glu Lys Glu Arg Phe Glu Glu
675 680 685

Ile Lys Glu Arg Leu Arg Val Leu Leu Glu Asn Gln Ile Thr His Phe
690 695 700

Arg Tyr Cys Phe Pro Phe Gly Arg Pro Glu Gly Ala Leu Lys Ala Thr
705 710 715 720

Leu Ser Leu Leu Glu Arg Val Leu Met Lys Asp Ile Val Thr Pro Val
725 730 735

Pro Gln Glu Glu Val Lys Thr Val Ile Arg Lys Cys Leu Glu Gln Ala
740 745 750

Ala Leu Val Asn Tyr Ser Arg Leu Ser Glu Tyr Ala Lys Ile Glu Glu
755 760 765

Asn Gln Lys Asp Ala Glu Asn Val Gly Arg Leu Ile Thr Pro Ala Lys
770 775 780

Lys Leu Glu Asp Thr Ile Arg Leu Ala Glu Leu Val Ile Glu Val Leu
785 790 795 800

Gln Gln Asn Glu Glu His His Ala Glu Gly Lys Glu Ala Phe Ala Trp
805 810 815

Trp Ser Asp Leu Met Val Glu His Ala Glu Thr Phe Leu Ser Leu Phe
820 825 830

Ala Val Asp Met Asp Ala Ala Leu Glu Val Gln Pro Pro Asp Thr Trp
835 840 845

Asp Ser Phe Pro Leu Phe Gln Leu Leu Asn Asp Phe Leu Arg Thr Asp
850 855 860

Tyr Asn Leu Cys Asn Gly Lys Phe His Lys His Leu Gln Asp Leu Phe
865 870 875 880

Ala Pro Leu Val Val Arg Tyr Val Asp Leu Met Glu Ser Ser Ile Ala
885 890 895

Gln Ser Ile His Arg Gly Phe Glu Arg Glu Ser Trp Glu Pro Val Asn
900 905 910

432

Asn Gly Ser Gly Thr Ser Glu Asp Leu Phe Trp Lys Leu Asp Ala Leu
915 920 925

Gln Thr Phe Ile Arg Asp Leu His Trp Pro Glu Glu Glu Phe Gly Lys
930 935 940

His Leu Glu Gln Arg Leu Lys Leu Met Ala Ser Asp Met Ile Glu Ser
945 950 955 960

Cys Val Lys Arg Thr Arg Ile Ala Phe Glu Val Lys Leu Gln Lys Thr
965 970 975

Ser Arg Ser Thr Asp Phe Arg Val Pro Gln Ser Ile Cys Thr Met Phe
980 985 990

Asn Val Met Val Asp Ala Lys Ala Gln Ser Thr Lys Leu Cys Ser Met
995 1000 1005

Glu Met Gly Gln Glu His Gln Tyr His Ser Lys Ile Asp Glu Leu
1010 1015 1020

Ile Glu Glu Thr Val Lys Glu Met Ile Thr Leu Leu Val Ala Lys
1025 1030 1035

Phe Val Thr Ile Leu Glu Gly Val Leu Ala Lys Leu Ser Arg Tyr
1040 1045 1050

Asp Glu Gly Thr Leu Phe Ser Ser Phe Leu Ser Phe Thr Val Lys
1055 1060 1065

Ala Ala Ser Lys Tyr Val Asp Val Pro Lys Pro Gly Met Asp Val
1070 1075 1080

Ala Asp Ala Tyr Val Thr Phe Val Arg His Ser Gln Asp Val Leu
1085 1090 1095

Arg Asp Lys Val Asn Glu Glu Met Tyr Ile Glu Arg Leu Phe Asp
1100 1105 1110

Gln Trp Tyr Asn Ser Ser Met Asn Val Ile Cys Thr Trp Leu Thr
1115 1120 1125

Asp Arg Met Asp Leu Gln Leu His Ile Tyr Gln Leu Lys Thr Leu
1130 1135 1140

Ile Arg Met Val Lys Lys Thr Tyr Arg Asp Phe Arg Leu Gln Gly
1145 1150 1155

Val Leu Asp Ser Thr Leu Asn Ser Lys Thr Tyr Glu Thr Ile Arg
1160 1165 1170

Asn Arg Leu Thr Val Glu Glu Ala Thr Ala Ser Val Ser Glu Gly
1175 1180 1185

Gly Gly Leu Gln Gly Ile Ser Met Lys Asp Ser Asp Glu Glu Asp
1190 1195 1200

Glu Glu Asp Asp
1205

<210> 206

433

<211> 1018
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<400> 206
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 Ala Ala Gln Ile Arg Arg Glu Leu Asp Gly Arg Leu Gln Leu Ala Asp
 35 40 45
 Lys Met Ala Lys Glu Arg Lys Phe Pro Lys Phe Ile Ala Lys Asp Met
 50 55 60
 Glu Asn Met Tyr Ile Glu Glu Leu Arg Ser Ser Val Asn Leu Leu Met
 65 70 75 80
 Ala Asn Leu Glu Ser Leu Pro Val Ser Lys Gly Gly Pro Glu Phe Lys
 85 90 95
 Leu Gln Lys Leu Lys Arg Ser Gln Asn Ser Ala Phe Leu Asp Ile Gly
 100 105 110
 Asp Glu Asn Glu Ile Gln Leu Ser Lys Ser Asp Val Val Leu Ser Phe
 115 120 125
 Thr Leu Glu Ile Val Ile Met Glu Val Gln Gly Leu Lys Ser Val Ala
 130 135 140
 Pro Asn Arg Ile Val Tyr Cys Thr Met Glu Val Glu Gly Glu Lys Leu
 145 150 155 160
 Gln Thr Asp Gln Ala Glu Ala Ser Arg Pro Gln Trp Gly Thr Gln Gly
 165 170 175
 Asp Phe Thr Thr Thr His Pro Arg Pro Val Val Lys Val Lys Leu Phe
 180 185 190
 Thr Glu Ser Thr Gly Val Leu Ala Leu Glu Asp Lys Glu Leu Gly Arg
 195 200 205
 Val Ile Leu Tyr Pro Thr Ser Asn Ser Ser Lys Ser Ala Glu Leu His
 210 215 220
 Arg Met Val Val Pro Lys Asn Ser Gln Asp Ser Asp Leu Lys Ile Lys
 225 230 235 240
 Leu Ala Val Arg Met Asp Lys Pro Ala His Met Lys His Ser Gly Tyr
 245 250 255
 Leu Tyr Ala Leu Gly Gln Lys Val Trp Lys Arg Trp Lys Lys Arg Tyr
 260 265 270
 Phe Val Leu Val Gln Val Ser Gln Tyr Thr Phe Ala Met Cys Ser Tyr
 275 280 285
 Arg Glu Lys Lys Ser Glu Pro Gln Glu Leu Met Gln Leu Glu Gly Tyr
 290 295 300

434

Thr Val Asp Tyr Thr Asp Pro His Pro Gly Leu Gln Gly Gly Cys Met
 305 310 315
 Phe Phe Asn Ala Val Lys Glu Gly Asp Thr Val Ile Phe Ala Ser Asp
 325 330 335
 Asp Glu Gln Asp Arg Ile Leu Trp Val Gln Ala Met Tyr Arg Ala Thr
 340 345 350
 Gly Gln Ser Tyr Lys Pro Val Pro Ala Ile Gln Thr Gln Lys Leu Asn
 355 360 365
 Pro Lys Gly Gly Thr Leu His Ala Asp Ala Gln Leu Tyr Ala Asp Arg
 370 375 380
 Phe Gln Lys His Gly Met Asp Glu Phe Ile Ser Ala Asn Pro Cys Lys
 385 390 395 400
 Leu Asp His Ala Phe Leu Phe Arg Ile Leu Gln Arg Gln Thr Leu Asp
 405 410 415
 His Arg Leu Asn Asp Ser Tyr Ser Cys Leu Gly Trp Phe Ser Pro Gly
 420 425 430
 Gln Val Phe Val Leu Asp Glu Tyr Cys Ala Arg Tyr Gly Val Arg Gly
 435 440 445
 Cys His Arg His Leu Cys Tyr Leu Ala Glu Leu Met Glu His Ser Glu
 450 455 460
 Asn Gly Ala Val Ile Asp Pro Thr Leu Leu His Tyr Ser Phe Ala Phe
 465 470 475 480
 Cys Ala Ser His Val His Gly Asn Arg Pro Asp Gly Ile Gly Thr Val
 485 490 495
 Ser Val Glu Glu Lys Glu Arg Phe Glu Glu Ile Lys Glu Arg Leu Ser
 500 505 510
 Ser Leu Leu Glu Asn Gln Ile Ser His Phe Arg Tyr Cys Phe Pro Phe
 515 520 525
 Gly Arg Pro Glu Gly Ala Leu Lys Ala Thr Leu Ser Leu Leu Glu Arg
 530 535 540
 Val Leu Met Lys Asp Ile Ala Thr Pro Ile Pro Ala Glu Glu Val Lys
 545 550 555 560
 Lys Val Val Arg Lys Cys Leu Glu Lys Ala Ala Leu Ile Asn Tyr Thr
 565 570 575
 Arg Leu Thr Glu Tyr Ala Lys Ile Glu Glu Thr Met Asn Gln Ala Ser
 580 585 590
 Pro Ala Arg Lys Leu Glu Glu Ile Leu His Leu Ala Glu Leu Cys Ile
 595 600 605
 Glu Val Leu Gln Gln Asn Glu Glu His His Ala Glu Ala Phe Ala Trp
 610 615 620
 Trp Pro Asp Leu Leu Ala Glu His Ala Glu Lys Phe Trp Ala Leu Phe
 625 630 635 640

435

Thr Val Asp Met Asp Thr Ala Leu Glu Ala Gln Pro Gln Asp Ser Trp 645 650 655
 Asp Ser Phe Pro Leu Phe Gln Leu Leu Asn Asn Phe Leu Arg Asn Asp 660 665 670
 Thr Leu Leu Cys Asn Gly Lys Phe His Lys His Leu Gln Gln Ile Phe 675 680 685
 Val Pro Leu Val Val Arg Tyr Val Asp Leu Met Glu Ser Ser Ile Ala 690 695 700
 Gln Ser Ile His Arg Gly Phe Glu Gln Glu Thr Trp Gln Pro Val Asn 705 710 715 720
 Asn Gly Ser Ala Thr Ser Glu Asp Leu Phe Thr Trp Lys Leu Asp Ala Leu 725 730 735
 Gln Met Phe Val Phe Asp Leu His Trp Pro Glu Gln Glu Phe Ala His 740 745 750
 His Leu Glu Gln Arg Leu Lys Leu Met Ala Ser Asp Met Leu Glu Ala 755 760 765
 Cys Val Lys Arg Thr Arg Thr Ala Phe Glu Leu Lys Leu Gln Lys Ala 770 775 780
 Ser Lys Thr Thr Asp Leu Arg Ile Pro Ala Ser Val Cys Thr Met Phe 785 790 795 800
 Asn Val Leu Val Asp Ala Lys Lys Gln Ser Thr Lys Leu Cys Ala Leu 805 810 815
 Asp Gly Gly Gln Glu Phe Gly Ser Gln Trp Gln Gln Tyr His Ser Lys 820 825 830
 Ile Asp Asp Leu Ile Asp Asn Ser Val Lys Glu Ile Ile Ser Leu Leu 835 840 845
 Val Ser Lys Phe Val Ser Val Leu Glu Gly Val Leu Ser Lys Leu Ser 850 855 860
 Arg Tyr Asp Glu Gly Thr Phe Phe Ser Ser Ile Leu Ser Phe Thr Val 865 870 875 880
 Lys Ala Ala Lys Tyr Val Asp Val Pro Lys Pro Gly Met Asp Leu 885 890 895
 Ala Asp Thr Tyr Ile Met Phe Val Arg Gln Asn Gln Asp Ile Leu Arg 900 905 910
 Glu Lys Val Asn Glu Glu Met Tyr Ile Glu Lys Leu Phe Asp Gln Trp 915 920 925
 Tyr Ser Ser Ser Met Lys Val Ile Cys Val Trp Leu Thr Asp Arg Leu 930 935 940
 Asp Leu Gln Leu His Ile Tyr Gln Leu Lys Thr Leu Ile Lys Ile Val 945 950 955 960
 Lys Lys Thr Tyr Arg Asp Phe Arg Leu Gln Gly Val Leu Glu Gly Thr 965 970 975

Leu Asn Ser Lys Thr Tyr Asp Thr Val His Arg Arg Leu Thr Val Glu 980 985 990
 Glu Ala Thr Ala Ser Val Ser Glu Gly Gly Gly Leu Gln Gly Ile Thr 995 1000 1005
 Met Lys Asp Ser Asp Glu Glu Glu Glu Gly 1010 1015
 <210> 207
 <211> 591
 <212> PRT
 <213> Homo sapiens
 <400> 207
 Met Ser Ser Leu Ser Ala Leu Phe Ser Val Ser Asp Lys Thr Gly Leu 1 5 10 15
 Val Glu Phe Ala Arg Asn Leu Thr Ala Leu Gly Leu Asn Leu Val Ala 20 25 30
 Ser Gly Gly Thr Ala Lys Ala Leu Arg Asp Ala Gly Leu Ala Val Arg 35 40 45
 Asp Val Ser Glu Leu Thr Gly Phe Pro Glu Met Leu Gly Gly Arg Val 50 55 60
 Lys Thr Leu His Pro Ala Val His Ala Gly Ile Leu Ala Arg Asn Ile 65 70 75 80
 Pro Glu Asp Asn Ala Asp Met Ala Arg Leu Asp Phe Asn Leu Ile Arg 85 90 95
 Val Val Ala Cys Asn Leu Tyr Pro Phe Val Lys Thr Val Ala Ser Pro 100 105 110
 Gly Val Thr Val Glu Glu Ala Val Glu Gln Ile Asp Ile Gly Gly Val 115 120 125
 Thr Leu Leu Arg Ala Ala Lys Asn His Ala Arg Val Thr Val Val 130 135 140
 Cys Glu Pro Glu Asp Tyr Val Val Val Ser Thr Glu Met Gln Ser Ser 145 150 155 160
 Glu Ser Lys Gly Thr Ser Leu Glu Thr Arg Arg Gln Leu Ala Leu Lys 165 170 175
 Ala Phe Thr His Thr Ala Gln Tyr Asp Glu Ala Ile Ser Asp Tyr Phe 180 185 190
 Arg Lys Gln Tyr Ser Lys Gly Val Ser Gln Met Pro Leu Arg Tyr Gly 195 200 205
 Met Asn Pro His Gln Thr Pro Ala Gln Leu Tyr Thr Leu Gln Pro Lys 210 215 220
 Leu Pro Ile Thr Val Leu Asn Gly Ala Pro Gly Phe Ile Asn Leu Cys 225 230 235 240

Asp Ala Leu Asn Ala Trp Gln Leu Val Lys Glu Leu Lys Glu Ala Leu 255
 245
 Gly Ile Pro Ala Ala Ser Phe Lys His Val Ser Pro Ala Gly Ala 270
 260
 Ala Val Gly Ile Pro Leu Ser Glu Asp Glu Ala Lys Val Cys Met Val 285
 275
 Tyr Asp Leu Tyr Lys Thr Leu Thr Pro Ile Ser Ala Ala Tyr Ala Arg 300
 290
 Ala Arg Gly Ala Asp Arg Met Ser Ser Phe Gly Asp Phe Val Ala Leu 320
 305
 Ser Asp Val Cys Asp Val Pro Thr Ala Lys Ile Ile Ser Arg Glu Val 335
 325
 Ser Asp Gly Ile Ile Ala Pro Gly Tyr Glu Glu Glu Ala Leu Thr Ile 350
 340
 Leu Ser Lys Lys Lys Asn Gly Asn Tyr Cys Val Leu Gln Met Asp Gln 365
 355
 Ser Tyr Lys Pro Asp Glu Asn Glu Val Arg Thr Leu Phe Gly Leu His 380
 370
 Leu Ser Gln Lys Arg Asn Asn Gly Val Val Asp Lys Ser Leu Phe Ser 400
 385
 Asn Val Val Thr Lys Asn Lys Asp Leu Pro Glu Ser Ala Leu Arg Asp 415
 405
 Leu Ile Val Ala Thr Ile Ala Val Lys Tyr Thr Gln Ser Asn Ser Val 430
 420
 Cys Tyr Ala Lys Asn Gly Gln Val Ile Gly Ile Gly Ala Gly Gln Gln 445
 435
 Ser Arg Ile His Cys Thr Arg Leu Ala Gly Asp Lys Ala Asn Tyr Trp 460
 450
 Trp Leu Arg His His Pro Gln Val Leu Ser Met Lys Phe Lys Thr Gly 480
 465
 Val Lys Arg Ala Glu Ile Ser Asn Ala Ile Asp Gln Tyr Val Thr Gly 495
 485
 Thr Ile Gly Glu Asp Glu Asp Leu Ile Lys Trp Lys Ala Leu Phe Glu 510
 500
 Glu Val Pro Glu Leu Leu Thr Glu Ala Glu Lys Lys Glu Trp Val Glu 525
 515
 Lys Leu Thr Glu Val Ser Ile Ser Ser Asp Ala Phe Phe Pro Phe Arg 540
 530
 Asp Asn Val Asp Arg Ala Lys Arg Ser Gly Val Ala Tyr Ile Ala Ala 560
 545
 Pro Ser Gly Ser Ala Ala Asp Lys Val Val Ile Glu Ala Cys Asp Glu 575
 565

438

Leu Gly Ile Ile Leu Ala His Thr Asn Leu Arg Leu Phe His His 590
 580
 <210> 208
 <211> 261
 <212> .PRT
 <213> Homo sapiens
 <400> 208
 Ala Pro Ala Leu Leu Leu Ile Pro Ala Ala Leu Ala Ser Phe Ile Leu 15
 1
 Ala Phe Gly Thr Gly Val Glu Phe Val Arg Phe Thr Ser Leu Arg Pro 30
 20
 Leu Leu Gly Gly Ile Pro Glu Ser Gly Gly Pro Asp Ala Arg Gln Gly 45
 35
 Trp Leu Ala Ala Leu Gln Asn Arg Ser Ile Leu Ala Pro Leu Ala Trp 60
 50
 Asp Leu Gly Leu Leu Leu Phe Val Gly Gln His Ser Leu Met Ala 80
 65
 Ala Glu Arg Val Lys Ala Trp Thr Ser Arg Tyr Phe Gly Val Leu Gln 95
 85
 Arg Ser Leu Tyr Val Ala Cys Thr Ala Leu Ala Leu Gln Leu Val Met 110
 100
 Arg Tyr Trp Glu Pro Ile Pro Lys Gly Pro Val Leu Trp Glu Ala Arg 125
 115
 Ala Glu Pro Trp Ala Thr Trp Val Pro Leu Leu Cys Phe Val Leu His 140
 130
 Val Ile Ser Trp Leu Leu Ile Phe Ser Ile Leu Leu Val Phe Asp Tyr 160
 145
 Ala Glu Leu Met Gly Leu Lys Gln Val Tyr Tyr His Val Leu Gly Leu 175
 165
 Gly Glu Pro Leu Ala Leu Lys Ser Pro Arg Ala Leu Arg Leu Phe Ser 190
 180
 His Leu Arg His Pro Val Cys Val Glu Leu Leu Thr Val Leu Trp Val 205
 195
 Val Pro Thr Leu Gly Thr Asp Arg Leu Leu Leu Ala Phe Leu Leu Thr 220
 210
 Leu Tyr Leu Gly Leu Ala His Gly Leu Asp Gln Gln Asp Leu Arg Tyr 240
 225
 Leu Arg Ala Gln Leu Gln Arg Lys Leu His Leu Leu Ser Arg Pro Gln 255
 245
 Asp Gly Glu Ala Glu 260
 <210> 209

439

<211> 623
 <212> PRT
 <213> Homo sapiens

<400> 209
 Met Glu Ser Tyr His Lys Pro Asp Gln Gln Lys Leu Gln Ala Leu Lys 15
 1 5 10 25 30
 Asp Thr Ala Asn Arg Leu Arg Ile Ser Ser Ile Gln Ala Thr Thr Ala 30
 20 25 30
 Ala Gly Ser Gly His Pro Thr Ser Cys Cys Ser Ala Ala Glu Ile Met 45
 35 40 45
 Ala Val Leu Phe Phe His Thr Met Arg Tyr Lys Ser Gln Asp Pro Arg 60
 50 55 60
 Asn Pro His Asn Asp Arg Phe Val Leu Ser Lys Gly His Ala Ala Pro 80
 65 70 75 80
 Ile Leu Tyr Ala Val Trp Ala Glu Ala Gly Phe Leu Ala Glu Ala Glu 95
 85 90 95
 Leu Leu Asn Leu Arg Lys Ile Ser Ser Asp Leu Asp Gly His Pro Val 110
 100 105 110
 Pro Lys Gln Ala Phe Thr Asp Val Ala Thr Gly Ser Leu Gly Gln Gly 125
 115 120 125
 Leu Gly Ala Ala Cys Gly Met Ala Tyr Thr Gly Lys Tyr Phe Asp Lys 140
 130 135 140
 Ala Ser Tyr Arg Val Tyr Cys Leu Leu Gly Asp Gly Glu Leu Ser Glu 160
 145 150 155 160
 Gly Ser Val Trp Glu Ala Met Ala Phe Ala Ser Ile Tyr Lys Leu Asp 175
 165 170 175
 Asn Leu Val Ala Ile Leu Asp Ile Asn Arg Leu Gly Gln Ser Asp Pro 190
 180 185 190
 Ala Pro Leu Gln His Gln Met Asp Ile Tyr Gln Lys Arg Cys Glu Ala 205
 195 200 205
 Phe Gly Trp His Ala Ile Ile Val Asp Gly His Ser Val Glu Glu Leu 220
 210 215 220
 Cys Lys Ala Phe Gly Gln Ala Lys His Gln Pro Thr Ala Ile Ile Ala 240
 225 230 235 240
 Lys Thr Phe Lys Gly Arg Gly Ile Thr Gly Val Glu Asp Lys Glu Ser 255
 245 250 255
 Trp His Gly Lys Pro Leu Pro Lys Asn Met Ala Glu Gln Ile Ile Gln 270
 260 265 270
 Glu Ile Tyr Ser Gln Ile Gln Ser Lys Lys Lys Ile Leu Ala Thr Pro 285
 275 280 285
 Pro Gln Glu Asp Ala Pro Ser Val Asp Ile Ala Asn Ile Arg Met Pro 300
 290 295 300

440

Ser Leu Pro Ser Tyr Lys Val Gly Asp Lys Ile Ala Thr Arg Lys Ala 320
 305 310 315 320
 Tyr Gly Gln Ala Leu Ala Lys Leu Gly His Ala Ser Asp Arg Ile Ile 335
 325 330 335
 Ala Leu Asp Gly Asp Thr Lys Asn Ser Thr Phe Ser Glu Ile Phe Lys 350
 340 345 350
 Lys Glu His Pro Asp Arg Phe Ile Glu Cys Tyr Ile Ala Glu Gln Asn 365
 355 360 365
 Met Val Ser Ile Ala Val Gly Cys Ala Thr Arg Asn Arg Thr Val Pro 380
 370 375 380
 Phe Cys Ser Thr Phe Ala Ala Phe Phe Thr Arg Ala Phe Asp Gln Ile 400
 385 390 395 400
 Arg Met Ala Ala Ile Ser Glu Ser Asn Ile Asn Leu Cys Gly Ser His 415
 405 410 415
 Cys Gly Val Ser Ile Gly Glu Asp Gly Pro Ser Gln Met Ala Leu Glu 430
 420 425 430
 Asp Leu Ala Met Phe Arg Ser Val Pro Thr Ser Thr Val Phe Tyr Pro 445
 435 440 445
 Ser Asp Gly Val Ala Thr Glu Lys Ala Val Glu Leu Ala Ala Asn Thr 460
 450 455 460
 Lys Gly Ile Cys Phe Ile Arg Thr Ser Arg Pro Glu Asn Ala Ile Ile 480
 465 470 475 480
 Tyr Asn Asn Asn Glu Asp Phe Gln Val Gly Gln Ala Lys Val Val Leu 495
 485 490 495
 Lys Ser Lys Asp Asp Gln Val Thr Val Ile Gly Ala Gly Val Thr Leu 510
 500 505 510
 His Glu Ala Leu Ala Ala Glu Leu Lys Lys Glu Lys Ile Asn 525
 515 520 525
 Ile Arg Val Leu Asp Pro Phe Thr Ile Lys Pro Leu Asp Arg Lys Leu 540
 530 535 540
 Ile Leu Asp Ser Ala Arg Ala Thr Lys Gly Arg Ile Leu Thr Val Glu 560
 545 550 555 560
 Asp His Tyr Tyr Glu Gly Gly Ile Gly Glu Ala Val Ser Ser Ala Val 575
 565 570 575
 Val Gly Glu Pro Gly Ile Thr Val Thr His Leu Ala Val Asn Arg Val 590
 580 585 590
 Pro Arg Ser Gly Lys Pro Ala Glu Leu Lys Met Phe Gly Ile Asp 605
 595 600 605
 Arg Asp Ala Ile Ala Gln Ala Val Arg Gly Leu Ile Thr Lys Ala 620
 610 615 620
 <210> 210
 <211> 772

441

<212> PRT
<213> Homo sapiens

<400> 210
1 Leu Cys Pro Tyr Leu Ser Pro Asp Ala Thr Gly Pro Ser Gly Leu Arg 15
5 Val Leu Pro Gln Gly Tyr Gly Trp Asn Leu Leu Tyr Gly Ser Leu Leu 30
20 Leu Gly Leu Val Gly Gly Val Cys Thr Leu Gly Ala Gly Leu Tyr Ala 45
35 Arg Ala Ser Phe Leu Thr Phe Leu Leu Val Ser Gly Ser Leu Ala Ser 60
50 Val Leu Ile Ser Phe Val Ala Val Gly Pro Arg Asp Ile Arg Leu Thr 80
65 Pro Arg Pro Gly Pro Asn Gly Ser Ser Leu Pro Pro Arg Phe Gly His 95
85 Phe Thr Gly Phe Asn Ser Ser Thr Leu Lys Asp Asn Leu Gly Ala Gly 110
100 Tyr Ala Glu Asp Tyr Thr Thr Gly Ala Val Met Asn Phe Ala Ser Val 125
115 Phe Ala Val Leu Phe Asn Gly Cys Thr Gly Ile Met Ala Gly Ala Asn 140
130 Met Ser Gly Glu Leu Lys Asp Pro Ser Arg Ala Ile Pro Leu Gly Thr 155
145 Ile Val Ala Val Ala Tyr Thr Phe Phe Val Tyr Val Leu Leu Phe Phe 175
165 Leu Ser Ser Phe Thr Cys Asp Arg Thr Leu Leu Gln Glu Asp Tyr Gly 190
180 Phe Phe Arg Ala Ile Ser Leu Trp Pro Pro Leu Val Leu Ile Gly Ile 205
195 Tyr Ala Thr Ala Leu Ser Ala Ser Met Ser Ser Leu Ile Gly Ala Ser 220
210 Arg Ile Leu His Ala Leu Ala Arg Asp Asp Leu Phe Gly Val Ile Leu 240
225 Ala Pro Ala Lys Val Val Ser Arg Gly Gly Asn Pro Trp Ala Ala Val 255
245 Leu Tyr Ser Trp Gly Leu Val Gln Leu Val Leu Leu Ala Gly Lys Leu 270
260 Asn Thr Leu Ala Ala Val Val Thr Val Phe Tyr Leu Val Ala Tyr Ala 285
275 Ala Val Asp Leu Ser Cys Leu Ser Leu Glu Trp Ala Ser Ala Pro Asn 300
290 Phe Arg Pro Thr Phe Ser Leu Phe Ser Trp His Thr Cys Leu Leu Gly

442

305 Val Ala Ser Cys Leu Leu Met Met Phe Leu Ile Ser Pro Gly Ala Ala 320
310 325 Gly Gly Ser Leu Leu Met Gly Leu Leu Ala Ala Leu Leu Thr Ala 335
340 Arg Gly Gly Pro Ser Ser Trp Gly Tyr Val Ser Gln Ala Leu Leu Phe 365
355 His Gln Val Arg Lys Tyr Leu Leu Arg Leu Asp Val Arg Lys Asp His 380
370 Val Lys Phe Trp Arg Pro Gln Leu Leu Val Gly Asn Pro Arg 400
385 Gly Ala Leu Pro Leu Leu Arg Leu Ala Asn Gln Leu Lys Lys Gly Gly 415
405 Leu Tyr Val Leu Gly His Val Thr Leu Gly Asp Leu Asp Ser Leu Pro 430
420 Ser Asp Pro Val Gln Pro Gln Tyr Gly Ala Trp Leu Ser Leu Val Asp 445
435 Arg Ala Gln Val Lys Ala Phe Val Asp Leu Thr Leu Ser Pro Ser Val 460
450 Arg Gln Gly Ala Gln His Leu Leu Arg Ile Ser Gly Leu Gly Gly Met 480
465 Lys Pro Asn Thr Leu Val Leu Gly Phe Tyr Asp Asp Ala Pro Pro Gln 495
485 Asp His Phe Leu Thr Asp Pro Ala Phe Ser Glu Pro Ala Asp Ser Thr 510
500 Arg Glu Gly Ser Ser Pro Ala Leu Ser Thr Leu Phe Pro Pro Arg 525
515 Ala Pro Gly Ser Pro Arg Ala Leu Asn Pro Gln Asp Tyr Val Ala Thr 540
530 Val Ala Asp Ala Leu Lys Met Asn Lys Asn Val Val Leu Ala Arg Ala 560
545 Ser Gly Ala Leu Pro Pro Glu Arg Leu Ser Arg Gly Ser Gly Gly Thr 575
565 Ser Gln Leu His His Val Asp Val Trp Pro Leu Asn Leu Leu Arg Pro 590
580 Arg Gly Gly Pro Gly Tyr Val Asp Val Cys Gly Leu Phe Leu Leu Gln 605
595 Met Ala Thr Ile Leu Gly Met Val Pro Ala Trp His Ser Ala Arg Leu 620
610 Arg Ile Phe Leu Cys Leu Gly Pro Arg Glu Ala Pro Gly Ala Ala Glu 640
625

443

Gly Arg Leu Arg Ala Leu Leu Ser Gln Leu Arg Ile Arg Ala Glu Val 645 650 655
 Gln Glu Val Val Trp Gly Glu Gly Ala Gly Ala Glu Pro Glu Ala 660 665 670
 Glu Glu Glu Gly Asp Phe Val Asn Ser Gly Arg Gly Asp Ala Glu Ala 675 680 685
 Glu Ala Leu Ala Arg Ser Ala Asn Ala Leu Val Arg Ala Gln Gln Gly 690 695 700
 Arg Gly Thr Gly Gly Pro Gly Gly Pro Glu Gly Gly Asp Ala Glu 705 710 715
 Gly Pro Ile Thr Ala Leu Thr Phe Leu Tyr Leu Pro Arg Pro Pro Ala 720 725 730
 Asp Pro Ala Arg Tyr Pro Arg Tyr Leu Ala Leu Leu Glu Thr Leu Thr 735 740 745
 Arg Asp Leu Gly Pro Thr Leu Leu Val His Gly Val Thr Pro Val Thr 750 755 760 765
 Cys Thr Asp Leu 770
 <210> 211
 <211> 820
 <212> PRT
 <213> Homo sapiens
 <400> 211
 Met Ala Gly Glu Leu Ala Asp Lys Lys Asp Arg Asp Ala Ser Pro Ser 1 5 10 15
 Lys Glu Glu Arg Lys Arg Ser Arg Thr Pro Asp Arg Glu Arg Asp Arg 20 25 30
 Asp Arg Asp Arg Lys Ser Ser Pro Ser Lys Asp Arg Lys Arg His Arg 35 40 45
 Ser Arg Asp Arg Arg Gly Gly Ser Arg Ser Arg Ser Arg Ser Arg 50 55 60
 Ser Lys Ser Ala Glu Arg Glu Arg Arg His Lys Glu Arg Glu Arg Asp 65 70 75 80
 Lys Glu Arg Asp Arg Asn Lys Lys Asp Arg Asp Arg Lys Asp Gly 85 90 95
 His Arg Arg Asp Lys Asp Arg Lys Arg Ser Ser Leu Ser Pro Gly Arg 100 105 110
 Gly Lys Asp Phe Lys Ser Arg Lys Asp Arg Asp Ser Lys Lys Asp Glu 115 120 125
 Glu Asp Glu His Gly Asp Lys Lys Pro Lys Ala Gln Pro Leu Ser Leu 130 135 140
 Glu Glu Leu Leu Ala Lys Lys Lys Ala Glu Glu Ala Glu Ala Lys 145 150 155 160

444

Pro Lys Phe Leu Ser Lys Ala Glu Arg Glu Ala Glu Ala Leu Lys Arg 165 170 175
 Arg Gln Gln Glu Val Glu Glu Arg Gln Arg Met Leu Glu Glu Arg 180 185 190
 Lys Lys Arg Lys Gln Phe Gln Asp Leu Gly Arg Lys Met Leu Glu Asp 195 200 205
 Pro Gln Glu Arg Glu Arg Arg Glu Arg Glu Arg Met Glu Arg Glu 210 215 220
 Thr Asn Gly Asn Glu Asp Glu Glu Gly Arg Gln Lys Ile Arg Glu Glu 225 230 235
 Lys Asp Lys Ser Lys Glu Leu His Ala Ile Lys Glu Arg Tyr Leu Gly 240 245 250 255
 Gly Ile Lys Lys Arg Arg Thr Arg His Leu Asn Asp Arg Lys Phe 260 265 270
 Val Phe Glu Trp Asp Ala Ser Glu Asp Thr Ser Ile Asp Tyr Asn Pro 275 280 285
 Leu Tyr Lys Glu Arg His Gln Val Gln Leu Leu Glu Gly Arg Gly Phe Ile 290 295 300
 Ala Gly Ile Asp Leu Lys Gln Gln Lys Arg Glu Gln Ser Arg Phe Tyr 305 310 315 320
 Gly Asp Leu Met Glu Lys Arg Arg Thr Leu Glu Glu Lys Glu Gln Glu 325 330 335
 Glu Ala Arg Leu Arg Lys Leu Arg Lys Lys Glu Ala Lys Gln Arg Trp 340 345 350
 Asp Asp Arg His Trp Ser Gln Lys Lys Leu Asp Glu Met Thr Asp Arg 355 360 365
 Asp Trp Arg Ile Phe Arg Glu Asp Tyr Ser Ile Thr Thr Lys Gly Gly 370 375 380
 Lys Ile Pro Asn Pro Ile Arg Ser Trp Lys Asp Ser Ser Leu Pro Pro 385 390 395 400
 His Ile Leu Glu Val Ile Asp Lys Lys Cys Gly Tyr Lys Glu Pro Thr Pro 405 410 415
 Ile Gln Arg Gln Ala Ile Pro Ile Gly Leu Gln Asn Arg Asp Ile Ile 420 425 430 435
 Gly Val Ala Glu Thr Gly Ser Gly Lys Thr Ala Ala Phe Leu Ile Pro 440 445
 Leu Leu Val Trp Ile Thr Thr Leu Pro Lys Ile Asp Arg Ile Glu Glu 450 455 460
 Ser Asp Gln Gly Pro Tyr Ala Ile Ile Leu Ala Pro Thr Arg Glu Leu 465 470 475 480
 Ala Gln Gln Ile Glu Glu Thr Ile Lys Phe Gly Lys Pro Leu Gly 485 490 495 500

445

485 490 495
 Ile Arg Thr Val Ala Val Ile Gly Gly Ile Ser Arg Glu Asp Gln Gly 500 510
 Phe Arg Leu Arg Met Gly Cys Glu Ile Val Ile Ala Thr Pro Gly Arg 515 520 525
 Leu Ile Asp Val Leu Glu Asn Arg Tyr Leu Val Leu Ser Arg Cys Thr 530 535 540
 Tyr Val Val Leu Asp Glu Ala Asp Arg Met Ile Asp Met Gly Phe Glu 545 550 555 560
 Pro Asp Val Gln Lys Ile Leu Glu His Met Pro Val Ser Asn Gln Lys 565 570 575
 Pro Asp Thr Asp Glu Ala Glu Asp Pro Glu Lys Met Leu Ala Asn Phe 580 585 590
 Glu Ser Gly Lys His Lys Tyr Arg Gln Thr Val Met Phe Thr Ala Thr 595 600 605
 Met Pro Pro Ala Val Glu Arg Leu Ala Arg Ser Tyr Leu Arg Arg Pro 610 615 620
 Ala Val Val Tyr Ile Gly Ser Ala Gly Lys Pro His Glu Arg Val Glu 625 630 635 640
 Gln Lys Val Phe Leu Met Ser Glu Ser Glu Lys Arg Lys Leu Leu 645 650 655
 Ala Ile Leu Glu Gln Gly Phe Asp Pro Pro Ile Ile Ile Phe Val Asn 660 665 670
 Gln Lys Lys Gly Cys Asp Val Leu Ala Lys Ser Leu Glu Lys Met Gly 675 680 685
 Tyr Asn Ala Cys Thr Leu His Gly Gly Lys Gly Gln Glu Gln Arg Glu 690 695 700
 Phe Ala Leu Ser Asn Leu Lys Ala Gly Ala Lys Asp Ile Leu Val Ala 705 710 715 720
 Thr Asp Val Ala Gly Arg Gly Ile Asp Ile Gln Asp Val Ser Met Val 725 730 735
 Val Asn Tyr Asp Met Ala Lys Asn Ile Glu Asp Tyr Ile His Arg Ile 740 745 750
 Gly Arg Thr Gly Arg Ala Gly Lys Ser Gly Val Ala Ile Thr Phe Leu 755 760 765
 Thr Lys Glu Asp Ser Ala Val Phe Tyr Glu Leu Lys Gln Ala Ile Leu 770 775 780
 Glu Ser Pro Val Ser Ser Cys Pro Pro Glu Leu Ala Asn His Pro Asp 785 790 795 800
 Ala Gln His Lys Pro Gly Thr Ile Leu Thr Lys Lys Arg Arg Glu Glu 805 810 815

Thr Ile Phe Ala 820
 <210> 212
 <211> 1032
 <212> PRT
 <213> Homo sapiens
 <400> 212
 Met Gly Arg Glu Ser Arg His Tyr Arg Lys Arg Ser Ala Ser Arg Gly 1 5 10 15
 Arg Ser Gly Ser Arg Ser Arg Ser Arg Ser Pro Ser Asp Lys Arg Ser 20 25 30
 Lys Arg Gly Asp Asp Arg Ser Arg Ser Arg Asp Arg Asp Arg Arg 35 40 45
 Arg Glu Arg Ser Arg Ser Arg Asp Lys Arg Arg Ser Arg Ser Arg Asp 50 55 60
 Arg Lys Arg Leu Arg Arg Ser Arg Ser Arg Glu Arg Asp Arg Ser Arg 65 70 75 80
 Glu Arg Arg Arg Ser Arg Ser Arg Asp Arg Arg Ser Arg Ser Arg 85 90 95
 Ser Arg Gly Arg Arg Ser Arg Ser Ser Ser Pro Gly Asn Lys Ser Lys 100 105 110
 Lys Thr Glu Asn Arg Ser Arg Ser Lys Glu Lys Thr Asp Gly Gly Glu 115 120 125
 Ser Ser Lys Glu Lys Lys Asp Lys Asp Lys Glu Asp Glu Lys 130 135 140
 Glu Lys Asp Ala Gly Asn Phe Asp Gln Asn Lys Leu Glu Glu Met 145 150 155 160
 Arg Lys Arg Lys Glu Arg Val Glu Lys Trp Arg Glu Glu Gln Arg Lys 165 170 175
 Lys Ala Met Glu Asn Ile Gly Glu Leu Lys Lys Glu Ile Glu Glu Met 180 185 190
 Lys Gln Gly Lys Lys Trp Ser Leu Glu Asp Asp Asp Asp Glu Asp 195 200 205
 Asp Pro Ala Glu Ala Glu Lys Glu Gly Asn Glu Met Glu Gly Glu Glu 210 215 220
 Leu Asp Pro Leu Asp Ala Tyr Met Glu Val Lys Glu Glu Val Lys 225 230 235 240
 Lys Phe Asn Met Arg Ser Val Lys Gly Gly Gly Asn Glu Lys Lys 245 250 255
 Ser Gly Pro Thr Thr Val Thr Lys Val Val Thr Val Thr Thr Lys Lys 260 265 270
 Ala Val Val Asp Ser Asp Lys Lys Gly Glu Leu Met Glu Asn Asp 275 280 285

Gln Asp Ala Met Glu Tyr Ser Ser Glu Glu Glu Val Asp Leu Gln
290 295 300
Thr Ala Leu Thr Gly Tyr Gln Thr Lys Gln Arg Lys Leu Leu Glu Pro
305 310 315 320
Val Asp His Gly Lys Ile Glu Tyr Glu Pro Phe Arg Lys Asn Phe Tyr
325 330 335
Val Glu Val Pro Glu Leu Ala Lys Met Ser Gln Glu Glu Val Asn Val
340 345 350
Phe Arg Leu Glu Met Glu Gly Ile Thr Val Lys Gly Lys Gly Cys Pro
355 360 365
Lys Pro Ile Lys Ser Trp Val Gln Cys Gly Ile Ser Met Lys Ile Leu
370 375 380
Asn Ser Leu Lys Lys His Gly Tyr Glu Lys Pro Thr Pro Ile Gln Thr
385 390 395 400
Gln Ala Ile Pro Ala Ile Met Ser Gly Arg Asp Leu Ile Gly Ile Ala
405 410 415
Lys Thr Gly Ser Gly Lys Thr Ile Ala Phe Leu Leu Pro Met Phe Arg
420 425 430
His Ile Met Asp Gln Arg Ser Leu Glu Gly Glu Gly Pro Ile Ala
435 440 445
Val Ile Met Thr Pro Thr Arg Glu Leu Ala Leu Gln Ile Thr Lys Glu
450 455 460
Cys Lys Lys Phe Ser Lys Thr Leu Gly Leu Arg Val Val Cys Val Tyr
465 470 475 480
Gly Gly Thr Gly Ile Ser Glu Gln Ile Ala Glu Leu Lys Arg Gly Ala
485 490 495
Glu Ile Ile Val Cys Thr Pro Gly Arg Met Ile Asp Met Leu Ala Ala
500 505 510
Asn Ser Gly Arg Val Thr Asn Leu Arg Arg Val Thr Tyr Val Val Leu
515 520 525
Asp Glu Ala Asp Arg Met Phe Asp Met Gly Phe Glu Pro Gln Val Met
530 535 540
Arg Ile Val Asp Asn Val Arg Pro Asp Arg Gln Thr Val Met Phe Ser
545 550 555 560
Ala Thr Phe Pro Arg Ala Met Glu Ala Leu Ala Arg Arg Ile Leu Ser
565 570 575
Lys Pro Ile Glu Val Gln Val Gly Gly Arg Ser Val Val Cys Ser Asp
580 585 590
Val Glu Gln Gln Val Ile Val Ile Glu Glu Glu Lys Phe Leu Lys
595 600 605
Leu Leu Glu Leu Leu Gly His Tyr Gln Glu Ser Gly Ser Val Ile Ile

448

610 615 620
Phe Val Asp Lys Gln Glu His Ala Asp Gly Leu Leu Lys Asp Leu Met
625 630 635 640
Arg Ala Ser Tyr Pro Cys Met Ser Leu His Gly Gly Ile Asp Gln Tyr
645 650 655
Asp Arg Asp Ser Ile Ile Asn Asp Phe Lys Asn Gly Thr Cys Lys Leu
660 665 670
Leu Val Ala Thr Ser Val Ala Ala Arg Gly Leu Asp Val Lys His Leu
675 680 685
Ile Leu Val Val Asn Tyr Ser Cys Pro Asn His Tyr Glu Asp Tyr Val
690 695 700
His Arg Ala Gly Arg Thr Gly Arg Ala Gly Asn Lys Gly Tyr Ala Tyr
705 710 715 720
Thr Phe Ile Thr Glu Asp Gln Ala Arg Tyr Ala Gly Asp Ile Ile Lys
725 730 735
Ala Leu Glu Leu Ser Gly Thr Ala Val Pro Asp Leu Glu Lys Leu
740 745 750
Trp Ser Asp Phe Lys Asp Gln Gln Lys Ala Glu Gly Lys Ile Ile Lys
755 760 765
Lys Ser Ser Gly Phe Ser Gly Lys Gly Phe Lys Phe Asp Glu Thr Glu
770 775 780
Gln Ala Leu Ala Asn Glu Arg Lys Lys Leu Gln Lys Ala Ala Leu Gly
785 790 795 800
Leu Gln Asp Ser Asp Asp Glu Asp Ala Ala Val Asp Ile Asp Glu Gln
805 810 815
Ile Glu Ser Met Phe Asn Ser Lys Lys Arg Val Lys Asp Met Ala Ala
820 825 830
Pro Gly Thr Ser Ser Val Pro Ala Pro Thr Ala Gly Asn Ala Glu Lys
835 840 845
Leu Glu Ile Ala Lys Arg Leu Ala Leu Arg Ile Asn Ala Gln Lys Asn
850 855 860
Leu Gly Ile Glu Ser Gln Val Asp Val Met Gln Gln Ala Thr Asn Ala
865 870 875 880
Ile Leu Arg Gly Gly Thr Ile Leu Ala Pro Thr Val Ser Ala Lys Thr
885 890 895
Ile Ala Glu Gln Leu Ala Glu Lys Ile Asn Ala Lys Leu Asn Tyr Val
900 905 910
Pro Leu Glu Lys Gln Glu Glu Arg Gln Asp Gly Gly Gln Asn Glu
915 920 925
Ser Phe Lys Arg Tyr Glu Glu Glu Leu Glu Ile Asn Asp Phe Pro Gln
930 935 940

449

Thr Ala Arg Trp Lys Val Thr Ser Lys Glu Ala Leu Gln Arg Ile Ser
 945 950 955 960
 Glu Tyr Ser Glu Ala Ala Ile Thr Ile Arg Gly Thr Tyr Phe Pro Pro
 965 970 975
 Gly Lys Glu Pro Lys Glu Gly Glu Arg Lys Ile Tyr Leu Ala Ile Glu
 980 985 990
 Ser Ala Asn Glu Leu Ala Val Gln Lys Ala Lys Ala Glu Ile Thr Arg
 995 1000 1005
 Leu Ile Lys Glu Glu Leu Ile Arg Leu Gln Asn Ser Tyr Gln Pro
 1010 1015 1020
 Thr Asn Lys Gly Arg Tyr Lys Val Leu
 1025 1030
 <210> 213
 <211> 437
 <212> PRT
 <213> Homo sapiens
 <400> 213
 Met Ala Thr Arg Ser Cys Arg Glu Lys Ala Gln Lys Leu Asn Glu Gln
 1 5 10 15
 His Gln Leu Ile Leu Ser Lys Leu Leu Arg Glu Asp Asn Lys Tyr
 20 25 30
 Cys Ala Asp Cys Glu Ala Lys Gly Pro Arg Trp Ala Ser Trp Asn Ile
 35 40 45
 Gly Val Phe Ile Cys Ile Arg Cys Ala Gly Ile His Arg Asn Leu Gly
 50 55 60
 Val His Ile Ser Arg Val Lys Ser Val Asn Leu Asp Gln Trp Thr Ala
 65 70 75 80
 Glu Gln Ile Gln Cys Met Gln Asp Met Gly Asn Thr Lys Ala Arg Leu
 85 90 95
 Leu Tyr Glu Ala Asn Leu Pro Glu Asn Phe Arg Arg Pro Gln Thr Asp
 100 105 110
 Gln Ala Val Glu Phe Phe Ile Arg Asp Lys Tyr Glu Lys Lys Lys Tyr
 115 120 125
 Tyr Asp Lys Asn Ala Ile Ala Ile Thr Asn Lys Glu Lys Glu Lys Lys
 130 135 140
 Lys Glu Glu Lys Lys Arg Glu Lys Glu Pro Glu Lys Pro Ala Lys Pro
 145 150 155 160
 Leu Thr Ala Glu Lys Leu Gln Lys Lys Asp Gln Gln Leu Glu Pro Lys
 165 170 175
 Lys Ser Thr Ser Pro Lys Lys Ala Ala Glu Pro Thr Val Asp Leu Leu
 180 185 190
 Gly Leu Asp Gly Pro Ala Val Ala Pro Val Thr Asn Gly Asn Thr Thr
 195 200 205
 450

Val Pro Pro Leu Asn Asp Asp Leu Asp Ile Phe Gly Pro Met Ile Ser
 210 215 220
 Asn Pro Leu Pro Ala Thr Val Met Pro Pro Ala Gln Gly Thr Pro Ser
 225 230 235 240
 Ala Pro Ala Ala Ala Thr Leu Ser Thr Val Thr Ser Gly Asp Leu Asp
 245 250 255
 Leu Phe Thr Glu Gln Thr Thr Lys Ser Glu Glu Val Ala Lys Lys Gln
 260 265 270
 Leu Ser Lys Asp Ser Ile Leu Ser Leu Tyr Gly Thr Gly Thr Ile Gln
 275 280 285
 Gln Gln Ser Thr Pro Gly Val Phe Met Gly Pro Thr Asn Ile Pro Phe
 290 295 300
 Thr Ser Gln Ala Pro Ala Ala Phe Gln Gly Phe Pro Ser Met Gly Val
 305 310 315 320
 Pro Val Pro Ala Ala Pro Gly Leu Ile Gly Asn Val Met Gly Gln Ser
 325 330 335
 Pro Ser Met Met Val Gly Met Pro Met Pro Asn Gly Phe Met Gly Asn
 340 345 350
 Ala Gln Thr Gly Val Met Pro Leu Pro Gln Asn Val Val Gly Pro Gln
 355 360 365
 Gly Gly Met Val Gly Gln Met Gly Ala Pro Gln Ser Lys Phe Gly Leu
 370 375 380
 Pro Gln Ala Gln Gln Pro Gln Trp Ser Leu Ser Gln Ile Met Gln Lys
 385 390 395 400
 Gly Asp Ala Val Leu Gln His Ser Ile Ile Ser Ala Ile Tyr Trp Pro
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 Thr Thr Arg Trp Leu Lys Cys Pro Leu Val Asp Glu Ser Ala Asp Gly
 420 425 430
 Trp His Glu Tyr Gln
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 <213> Homo sapiens
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 20 25 30
 Gly Ile His Arg Asn Leu Gly Val His Ile Ser Arg Val Lys Ser Val
 35 40 45
 Asn Leu Asp Gln Trp Thr Gln Glu Ile Gln Cys Met Gln Glu Met
 451

50 55 60
 Gly Asn Gly Lys Ala Asn Arg Leu Tyr Glu Ala Tyr Leu Pro Glu Thr 80
 65 70 75
 Phe Arg Arg Pro Gln Ile Asp Pro Ala Val Glu Gly Phe Ile Arg Asp 95
 85 90
 Lys Tyr Glu Lys Lys Tyr Met Asp Arg Ser Leu Asp Ile Asn Ala 110
 100 105
 Phe Arg Lys Glu Lys Asp Asp Lys Trp Lys Arg Gly Ser Glu Pro Val 125
 115 120
 Pro Glu Lys Lys Leu Glu Pro Val Phe Glu Lys Val Lys Met Pro 140
 130 135
 Gln Lys Lys Glu Asp Pro Gln Leu Pro Arg Lys Ser Ser Pro Lys Ser 160
 145 150 155
 Thr Ala Pro Val Met Asp Leu Leu Gly Leu Asp Ala Pro Val Ala Cys 175
 165 170
 Ser Ile Ala Asn Ser Lys Thr Ser Asn Thr Leu Glu Lys Asp Leu Asp 190
 180 185
 Leu Leu Ala Ser Val Pro Ser Pro Ser Ser Gly Ser Arg Lys Val 205
 195 200
 Val Gly Ser Met Pro Thr Ala Gly Ser Ala Gly Ser Val Pro Glu Asn 220
 210 215
 Leu Asn Leu Phe Pro Glu Pro Gly Ser Lys Ser Glu Glu Ile Gly Lys 240
 225 230 235
 Lys Gln Leu Ser Lys Asp Ser Ile Leu Ser Leu Tyr Gly Ser Gln Thr 255
 245 250
 Pro Gln Met Pro Thr Gln Ala Met Phe Met Ala Pro Ala Gln Met Ala 270
 260 265
 Tyr Pro Thr Ala Tyr Pro Ser Phe Pro Gly Val Thr Pro Pro Asn Ser 285
 275 280
 Ile Met Gly Ser Met Met Pro Pro Pro Val Gly Met Val Ala Gln Pro 300
 290 295
 Gly Ala Ser Gly Met Val Ala Pro Met Ala Met Pro Ala Gly Tyr Met 320
 305 310 315
 Gly Gly Met Gln Ala Ser Met Met Gly Val Pro Asn Gly Met Met Thr 335
 325 330
 Thr Gln Gln Ala Gly Tyr Met Ala Gly Met Ala Ala Met Pro Gln Thr 350
 340 345
 Val Tyr Gly Val Gln Pro Ala Gln Gln Leu Gln Trp Asn Leu Thr Gln 365
 355 360
 Met Thr Gln Gln Met Ala Gly Met Asn Phe Tyr Gly Ala Asn Gly Met 380
 370 375

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 Gln Thr Leu Ser Pro Gln Met Trp Lys 405
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 <211> 473
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 35 40
 Pro Val Gly Lys Phe Leu Gly Asp Ser Ala Asn Leu Ser Ile Leu Ser 60
 50 55
 Gly Gly Thr Pro Lys Cys Cys Leu Asp Leu Ser Asn Leu Ser Ser Gly 80
 65 70 75
 Glu Ile Thr Ala Thr Gln Leu Thr Thr Ser Ala Asp Leu Asp Glu Thr 95
 85 90
 Gly His Leu Asp Ser Ser Gly Leu Gln Glu Val His Leu Ala Gly Met 110
 100 105
 Asn His Asp Gln His Leu Met Lys Cys Ser Pro Ala Gln Leu Leu Cys 125
 115 120
 Ser Thr Pro Asn Gly Leu Asp Arg Gly His Arg Lys Arg Asp Ala Met 140
 130 135
 Cys Ser Ser Ala Asn Lys Glu Asn Asp Asn Gly Asn Leu Val Asp 160
 145 150 155
 Ser Glu Met Lys Tyr Leu Gly Ser Pro Ile Thr Thr Val Pro Lys Leu 175
 165 170
 Asp Lys Asn Pro Asn Leu Gly Glu Asp Gln Ala Glu Glu Ile Ser Asp 190
 180 185
 Glu Leu Met Glu Phe Ser Leu Lys Asp Gln Glu Ala Lys Val Ser Arg 205
 195 200
 Ser Gly Leu Tyr Arg Ser Pro Ser Met Pro Glu Asn Leu Asn Arg Pro 220
 210 215
 Arg Leu Lys Gln Val Glu Lys Phe Lys Asp Asn Thr Ile Pro Asp Lys 240
 225 230 235
 Val Lys Lys Lys Tyr Phe Ser Gly Gln Gly Lys Leu Arg Lys Gly Leu 255
 245 250
 Cys Leu Lys Lys Thr Val Ser Leu Cys Asp Ile Thr Ile Thr Gln Met 270
 260 265

Leu Glu Glu Asp Ser Asn Gln Gln His Leu Ile Gly Asp Phe Ser Lys
 275 280 285
 Val Cys Ala Leu Pro Thr Val Ser Gly Lys His Gln Asp Leu Lys Tyr
 290 295 300
 Val Asn Pro Glu Thr Val Ala Ala Leu Leu Ser Gly Lys Phe Gln Gly
 305 310 315 320
 Leu Ile Glu Lys Phe Tyr Val Ile Asp Cys Arg Tyr Pro Tyr Glu Tyr
 325 330 335
 Leu Gly Gly His Ile Gln Gly Ala Leu Asn Leu Tyr Ser Gln Glu Glu
 340 345 350
 Leu Phe Asn Phe Phe Leu Lys Lys Pro Ile Val Pro Leu Asp Thr Gln
 355 360 365
 Lys Arg Ile Ile Ile Val Phe His Cys Glu Phe Ser Ser Glu Arg Gly
 370 375 380
 Pro Arg Met Cys Arg Cys Leu Arg Glu Glu Asp Arg Ser Leu Asn Gln
 385 390 395 400
 Tyr Pro Ala Leu Tyr Tyr Pro Glu Leu Tyr Ile Leu Lys Gly Tyr
 405 410 415
 Arg Asp Phe Phe Pro Glu Tyr Met Glu Leu Cys Glu Pro Gln Ser Tyr
 420 425 430
 Cys Pro Met His His Gln Asp His Lys Thr Glu Leu Leu Arg Cys Arg
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 465 470
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 <211> 601
 <212> PRT
 <213> Homo sapiens
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 35 40 45
 Ser Ser Pro Val Thr Thr Leu Thr Gln Thr Met His Asp Leu Ala Gly
 50 55 60
 Leu Gly Ser Arg Ser Arg Leu Thr His Leu Ser Leu Ser Arg Arg Ala
 65 70 75 80
 Ser Glu Ser Ser Leu Ser Ser Glu Ser Ser Glu Ser Ser Asp Ala Gly

454

85 90 95
 Leu Cys Met Asp Ser Pro Ser Pro Met Asp Pro His Met Ala Glu Gln
 100 105 110
 Thr Phe Glu Gln Ala Ile Gln Ala Ala Ser Arg Ile Ile Arg Asn Glu
 115 120 125
 Gln Phe Ala Ile Arg Arg Phe Gln Ser Met Pro Val Arg Leu Leu Gly
 130 135 140
 His Ser Pro Val Leu Arg Asn Ile Thr Asn Ser Gln Ala Pro Asp Gly
 145 150 155 160
 Arg Arg Lys Ser Glu Ala Gly Ser Gly Ala Ala Ser Ser Ser Gly Glu
 165 170 175
 Asp Lys Glu Asn Val Arg Phe Thr Lys Ala Gly Val Gly Ala Leu Arg
 180 185 190
 Glu Glu Glu Gly Ala Cys Tyr Gly Gly Ser Leu Ala Cys Glu Asp Pro
 195 200 205
 Pro Leu Pro Ser Trp Leu Gln Asp Gly Phe Val Phe Lys Met Pro Trp
 210 215 220
 Lys Pro Thr His Pro Ser Ser Thr His Ala Leu Ala Glu Trp Ala Ser
 225 230 235 240
 Arg Arg Glu Ala Phe Ala Gln Arg Pro Ser Ser Ala Pro Asp Leu Met
 245 250 255
 Cys Leu Ser Pro Asp Arg Lys Met Glu Val Glu Leu Ser Pro Leu
 260 265 270
 Ala Leu Gly Arg Phe Ser Leu Thr Pro Ala Glu Gly Asp Thr Glu Glu
 275 280 285
 Asp Asp Gly Phe Val Asp Ile Leu Glu Ser Asp Leu Lys Asp Asp
 290 295 300
 Ala Val Pro Pro Gly Met Glu Ser Leu Ile Ser Ala Pro Leu Val Lys
 305 310 315 320
 Thr Leu Glu Lys Glu Glu Glu Lys Asp Leu Val Met Tyr Ser Lys Cys
 325 330 335
 Gln Arg Leu Phe Arg Ser Pro Ser Met Pro Cys Ser Val Ile Arg Pro
 340 345 350
 Ile Leu Lys Arg Leu Glu Arg Pro Gln Asp Arg Asp Thr Pro Val Gln
 355 360 365
 Asn Lys Arg Arg Arg Ser Val Thr Pro Pro Glu Gln Gln Glu Ala
 370 375 380
 Glu Glu Pro Lys Ala Arg Val Leu Arg Ser Lys Ser Leu Cys His Asp
 385 390 395 400
 Glu Ile Glu Asn Leu Leu Asp Ser Asp His Arg Glu Leu Ile Gly Asp
 405 410 415

455

Tyr Ser Lys Ala Phe Leu Leu Gln Thr Val Asp Gly Lys His Gln Asp
 420 425
 Leu Lys Tyr Ile Ser Pro Glu Thr Met Val Ala Leu Leu Thr Gly Lys
 435 440
 Phe Ser Asn Ile Val Asp Lys Phe Val Ile Val Asp Cys Arg Tyr Pro
 450 455
 Tyr Glu Tyr Glu Gly His Ile Lys Thr Ala Val Asn Leu Pro Leu
 465 470
 Glu Arg Asp Ala Glu Ser Phe Leu Leu Lys Ser Pro Ile Ala Pro Cys
 485 490
 Ser Leu Asp Lys Arg Val Ile Leu Ile Phe His Cys Glu Phe Ser Ser
 500 505
 Glu Arg Gly Pro Arg Met Cys Arg Phe Ile Arg Glu Arg Asp Arg Ala
 515 520
 Val Asn Asp Tyr Pro Ser Leu Tyr Tyr Pro Glu Met Tyr Ile Leu Lys
 530 535
 Gly Gly Tyr Lys Glu Phe Phe Pro Gln His Pro Asn Phe Cys Glu Pro
 545 550
 Gln Asp Tyr Arg Pro Met Asn His Glu Ala Phe Lys Asp Glu Leu Lys
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 Glu Leu Cys Ser Arg Leu Gln Asp Gln
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 35 40 45
 Asp Gln Leu Gln Gly Leu Gly Ser Asp Tyr Glu Gln Pro Leu Glu Val
 50 55 60
 Lys Asn Asn Ser Asn Leu Gln Arg Met Gly Ser Ser Glu Ser Thr Asp
 65 70 75 80
 Ser Gly Phe Cys Leu Asp Ser Pro Gly Pro Leu Asp Ser Lys Glu Asn
 85 90 95
 Leu Glu Asn Pro Met Arg Arg Ile His Ser Leu Pro Gln Lys Leu Leu
 100 105 110

456

Gly Cys Ser Pro Ala Leu Lys Arg Ser His Ser Asp Ser Leu Asp His
 115 120
 Asp Ile Phe Gln Leu Ile Asp Pro Asp Glu Asn Lys Glu Asn Glu Ala
 130 135
 Phe Glu Phe Lys Lys Pro Val Arg Pro Val Ser Arg Gly Cys Leu His
 145 150
 Ser His Gly Leu Gln Glu Gly Lys Asp Leu Phe Thr Gln Arg Gln Asn
 165 170
 Ser Ala Gln Leu Gly Met Leu Ser Ser Asn Glu Arg Asp Ser Ser Glu
 180 185
 Pro Gly Asn Phe Ile Pro Leu Phe Thr Pro Gln Ser Pro Val Thr Ala
 195 200
 Thr Leu Ser Asp Glu Asp Asp Gly Phe Val Asp Leu Leu Asp Gly Glu
 210 215
 Asn Leu Lys Asn Glu Glu Thr Pro Ser Cys Met Ala Ser Leu Trp
 225 230
 Thr Ala Pro Leu Val Met Arg Thr Thr Asn Leu Asp Asn Arg Cys Lys
 245 250
 Leu Phe Asp Ser Pro Ser Leu Cys Ser Ser Thr Arg Ser Val Leu
 260 265
 Lys Arg Pro Glu Arg Ser Gln Glu Ser Pro Pro Gly Ser Thr Lys
 275 280
 Arg Arg Lys Ser Met Ser Gly Ala Ser Pro Lys Glu Ser Thr Asn Pro
 290 295
 Glu Lys Ala His Glu Thr Leu His Gln Ser Leu Ser Leu Ala Ser Ser
 305 310
 Pro Lys Gly Thr Ile Glu Asn Ile Leu Asp Asn Asp Pro Arg Asp Leu
 325 330
 Ile Gly Asp Phe Ser Lys Gly Tyr Leu Phe His Thr Val Ala Gly Lys
 340 345
 His Gln Asp Leu Lys Tyr Ile Ser Pro Glu Ile Met Ala Ser Val Leu
 355 360
 Asn Gly Lys Phe Ala Asn Leu Ile Lys Glu Phe Val Ile Ile Asp Cys
 370 375
 Arg Tyr Pro Tyr Glu Tyr Glu Gly His Ile Lys Gly Ala Val Asn
 385 390
 Leu His Met Glu Glu Val Glu Asp Phe Leu Leu Lys Lys Pro Ile
 405 410
 Val Pro Thr Asp Gly Lys Arg Val Ile Val Val Phe His Cys Glu Phe
 420 425
 Ser Ser Glu Arg Gly Pro Arg Met Cys Arg Tyr Val Arg Glu Asp

457

435 440 445
 Arg Leu Gly Asn Glu Tyr Pro Lys Leu His Tyr Pro Glu Leu Tyr Val 460
 450
 Leu Lys Gly Gly Tyr Lys Glu Phe Phe Met Lys Cys Gln Ser Tyr Cys 480
 465 470 475
 Glu Pro Pro Ser Tyr Arg Pro Met His His Glu Asp Phe Lys Glu Asp 495
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 500 505
 Lys Arg Glu Met Tyr Ser Arg Leu Lys Lys Leu 520
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 35 40
 Asp Gly Asp Val Phe Arg Phe Pro Gly Leu Cys Asp Tyr Asn Phe Ala 60
 50 55
 Ser Asp Cys Arg Gly Ser Tyr Lys Glu Phe Ala Val His Leu Lys Arg 80
 65 70 75
 Gly Pro Gly Gln Ala Glu Ala Pro Ala Gly Val Glu Ser Ile Leu Leu 95
 85 90
 Thr Ile Lys Asp Asp Thr Ile Tyr Leu Thr Arg His Leu Ala Val Leu 110
 100 105
 Asn Gly Ala Val Val Ser Thr Pro His Tyr Ser Pro Gly Leu Leu Ile 125
 115 120
 Glu Lys Ser Asp Ala Tyr Thr Lys Val Tyr Ser Arg Ala Gly Leu Thr 140
 130 135
 Leu Met Trp Asn Arg Glu Asp Ala Leu Met Leu Glu Leu Asp Thr Lys 160
 145 150 155
 Phe Arg Asn His Thr Cys Gly Leu Cys Gly Asp Tyr Asn Gly Leu Gln 175
 165 170
 Ser Tyr Ser Glu Phe Leu Ser Asp Gly Val Leu Phe Ser Pro Leu Glu 190
 180 185
 Phe Gly Asn Met Gln Lys Ile Asn Gln Pro Asp Val Val Cys Glu Asp 205
 195 200

458

Pro Glu Glu Glu Val Ala Pro Ala Ser Cys Ser Glu His Arg Ala Glu 220
 210 215
 Cys Glu Arg Leu Leu Thr Ala Glu Ala Phe Ala Asp Cys Gln Asp Leu 240
 225 230 235
 Val Pro Leu Glu Pro Tyr Leu Arg Ala Cys Gln Gln Asp Arg Cys Arg 255
 245 250
 Cys Pro Gly Gly Asp Thr Cys Val Cys Ser Thr Val Ala Glu Phe Ser 270
 260 265
 Arg Gln Cys Ser His Ala Gly Gly Arg Pro Gly Asn Trp Arg Thr Ala 285
 275 280
 Thr Leu Cys Pro Lys Thr Cys Pro Gly Asn Leu Val Tyr Leu Glu Ser 300
 290 295
 Gly Ser Pro Cys Met Asp Thr Cys Ser His Leu Glu Val Ser Ser Leu 320
 305 310 315
 Cys Glu Glu His Arg Met Asp Gly Cys Phe Cys Pro Glu Gly Thr Val 335
 325 330
 Tyr Asp Asp Ile Gly Asp Ser Gly Cys Val Pro Val Ser Gln Cys His 350
 340 345
 Cys Arg Leu His Gly His Leu Tyr Thr Pro Gly Gln Glu Ile Thr Asn 365
 355 360
 Asp Cys Glu Gln Cys Val Cys Asn Ala Gly Arg Trp Val Cys Lys Asp 380
 370 375
 Leu Pro Cys Pro Gly Thr Cys Ala Leu Glu Gly Gly Ser His Ile Thr 400
 385 390 395
 Thr Phe Asp Gly Lys Thr Tyr Thr Phe His Gly Asp Cys Tyr Tyr Val 415
 405 410
 Leu Ala Lys Gly Asp His Asn Asp Ser Tyr Ala Leu Leu Gly Glu Leu 430
 420 425
 Ala Pro Cys Gly Ser Thr Asp Lys Gln Thr Cys Leu Lys Thr Val Val 445
 435 440
 Leu Leu Ala Asp Lys Lys Lys Asn Ala Val Val Phe Lys Ser Asp Gly 460
 450 455
 Ser Val Leu Leu Asn Gln Leu Gln Val Asn Leu Pro His Val Thr Ala 480
 465 470 475
 Ser Phe Ser Val Phe Arg Pro Ser Ser Tyr His Ile Met Val Ser Met 495
 485 490
 Ala Ile Gly Val Arg Leu Gln Val Gln Leu Ala Pro Val Met Gln Leu 510
 500 505
 Phe Val Thr Leu Asp Gln Ala Ser Gln Gly Gln Val Gln Gly Leu Cys 525
 515 520
 Gly Asn Phe Asn Gly Leu Glu Gly Asp Phe Lys Thr Ala Ser Gly 540
 530 535

459

Leu Val Glu Ala Thr Gly Ala Gly Phe Ala Asn Thr Trp Lys Ala Gln 545 550 555
 Ser Thr Cys His Asp Lys Leu Asp Trp Leu Asp Asp Pro Cys Ser Leu 565 570 575
 Asn Ile Glu Ser Ala Asn Tyr Ala Glu His Trp Cys Ser Leu Leu Lys 580 585 590
 Lys Thr Glu Thr Pro Phe Gly Arg Cys His Ser Ala Val Asp Pro Ala 595 600 605
 Glu Tyr Tyr Lys Arg Cys Lys Tyr Asp Thr Cys Asn Cys Gln Asn Asn 610 615 620
 Glu Asp Cys Leu Cys Ala Ala Leu Ser Ser Tyr Ala Arg Ala Cys Thr 625 630 635 640
 Ala Lys Gly Val Met Leu Trp Gly Trp Arg Glu His Val Cys Asn Lys 645 650 655
 Asp Val Gly Ser Cys Pro Asn Ser Gln Val Phe Leu Tyr Asn Leu Thr 660 665 670
 Thr Cys Gln Gln Thr Cys Arg Ser Leu Ser Glu Ala Asp Ser His Cys 675 680 685
 Leu Glu Gly Phe Ala Pro Val Asp Gly Cys Gly Cys Pro Asp His Thr 690 695 700
 Phe Leu Asp Glu Lys Gly Arg Cys Val Pro Leu Ala Lys Cys Ser Cys 705 710 715 720
 Tyr His Arg Gly Leu Tyr Leu Glu Ala Gly Asp Val Val Val Arg Gln 725 730 735
 Glu Glu Arg Cys Val Cys Arg Asp Gly Arg Leu His Cys Arg Gln Ile 740 745 750
 Arg Leu Ile Gly Gln Ser Cys Thr Ala Pro Lys Ile His Met Asp Cys 755 760 765
 Ser Asn Leu Thr Ala Leu Ala Thr Ser Lys Pro Arg Ala Leu Ser Cys 770 775 780
 Gln Thr Leu Ala Ala Gly Tyr Tyr His Thr Glu Cys Val Ser Gly Cys 785 790 795 800
 Val Cys Pro Asp Gly Leu Met Asp Asp Gly Arg Gly Cys Val Val 805 810 815
 Glu Lys Glu Cys Pro Cys Val His Asn Asn Asp Leu Tyr Ser Ser Gly 820 825 830
 Ala Lys Ile Lys Val Asp Cys Asn Thr Cys Thr Cys Lys Arg Gly Arg 835 840 845
 Trp Val Cys Thr Gln Ala Val Cys His Gly Thr Cys Ser Ile Tyr Gly 850 855 860
 Ser Gly His Tyr Ile Thr Phe Asp Gly Lys Tyr Tyr Asp Phe Asp Gly

865 870 875 880
 His Cys Ser Tyr Val Ala Val Gln Asn Tyr Cys Gly Gln Asn Ser Ser 885 890 895
 Leu Gly Ser Phe Ser Ile Ile Thr Glu Asn Val Pro Cys Gly Thr Thr 900 905 910
 Gly Val Thr Cys Ser Lys Ala Ile Lys Ile Phe Met Gly Arg Thr Glu 915 920 925
 Leu Lys Leu Glu Asp Lys His Arg Val Val Ile Gln Arg Asp Glu Gly 930 935 940
 His His Val Ala Tyr Thr Thr Arg Glu Val Gly Gln Tyr Leu Val Val 945 950 955 960
 Glu Ser Ser Thr Gly Ile Ile Val Ile Trp Asp Lys Arg Thr Thr Val 965 970 975
 Phe Ile Lys Leu Ala Pro Ser Tyr Lys Gly Thr Val Cys Gly Leu Cys 980 985 990
 Gly Asn Phe Asp His Arg Ser Asn Asn Asp Phe Thr Thr Arg Asp His 995 1000 1005
 Met Val Val Ser Ser Glu Leu Asp Phe Gly Asn Ser Trp Lys Glu 1010 1015 1020
 Ala Pro Thr Cys Pro Asp Val Ser Thr Asn Pro Glu Pro Cys Ser 1025 1030 1035
 Leu Asn Pro His Arg Arg Ser Trp Ala Glu Lys Gln Cys Ser Ile 1040 1045 1050
 Leu Lys Ser Ser Val Phe Ser Ile Cys His Ser Lys Val Asp Pro 1055 1060 1065
 Lys Pro Phe Tyr Glu Ala Cys Val His Asp Ser Cys Ser Cys Asp 1070 1075 1080
 Thr Gly Gly Asp Cys Glu Cys Phe Cys Ser Ala Val Ala Ser Tyr 1085 1090 1095
 Ala Gln Glu Cys Thr Lys Glu Gly Ala Cys Val Phe Trp Arg Thr 1100 1105 1110
 Pro Asp Leu Cys Pro Ile Phe Cys Asp Tyr Tyr Asn Pro Pro His 1115 1120 1125
 Glu Cys Glu Trp His Tyr Glu Pro Cys Gly Asn Arg Ser Phe Glu 1130 1135 1140
 Thr Cys Arg Thr Ile Asn Gly Ile His Ser Asn Ile Ser Val Ser 1145 1150 1155
 Tyr Leu Glu Gly Cys Tyr Pro Arg Cys Pro Lys Asp Arg Pro Ile 1160 1165 1170
 Tyr Glu Glu Asp Leu Lys Cys Val Thr Ala Asp Lys Cys Gly 1175 1180 1185

Cys Tyr Val Glu Asp Thr His Tyr Pro Pro Gly Ala Ser Val Pro
 1190 1195 1200
 Thr Glu Glu Thr Cys Lys Ser Cys Val Cys Thr Asn Ser Ser Gln
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 Val Val Cys Arg Pro Glu Glu Gly Lys Ile Leu Asn Gln Thr Gln
 1225 1230
 Asp Gly Ala Phe Cys Tyr Trp Glu Ile Cys Gly Pro Asn Gly Thr
 1235 1240 1245
 Val Glu Lys His Phe Asn Ile Cys Ser Ile Thr Thr Arg Pro Ser
 1250 1255 1260
 Thr Leu Thr Thr Phe Thr Thr Ile Thr Leu Pro Thr Thr Pro Thr
 1265 1270 1275
 Ser Phe Thr Thr Thr Thr Thr Thr Thr Thr Ser Ser Thr
 1280 1285 1290
 Val Leu Ser Thr Thr Pro Lys Leu Cys Cys Leu Trp Ser Asp Trp
 1295 1300 1305
 Ile Asn Glu Asp His Pro Ser Ser Gly Ser Asp Asp Gly Asp Arg
 1310 1315 1320
 Glu Pro Phe Asp Gly Val Cys Gly Ala Pro Glu Asp Ile Glu Cys
 1325 1330 1335
 Arg Ser Val Lys Asp Pro His Leu Ser Leu Glu Gln His Gly Gln
 1340 1345 1350
 Lys Val Gln Cys Asp Val Ser Val Gly Phe Ile Cys Lys Asn Glu
 1355 1360 1365
 Asp Gln Phe Gly Asn Gly Pro Phe Gly Leu Cys Tyr Asp Tyr Lys
 1370 1375 1380
 Ile Arg Val Asn Cys Cys Trp Pro Met Asp Lys Cys Ile Thr Thr
 1385 1390 1395
 Pro Ser Pro Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr
 1400 1405 1410
 Thr Thr Leu Pro Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr
 1415 1420 1425
 Thr Thr Thr Pro Pro Pro Thr Thr Thr Pro Ser Pro Ile Thr
 1430 1435 1440
 Thr Thr Thr Thr Pro Leu Pro Thr Thr Thr Pro Ser Pro Pro Ile
 1445 1450 1455
 Ser Thr Thr Thr Thr Pro Pro Pro Thr Thr Thr Thr Ser Pro Pro
 1460 1465 1470
 Thr Thr Thr Pro Ser Pro Thr Thr Thr Thr Pro Ser Pro Thr Thr
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 Thr Thr Thr Thr Thr Pro Pro Thr Thr Thr Thr Thr Ser Pro Pro
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Met Thr Thr Pro Ile Thr Pro Pro Ala Ser Thr Thr Thr Thr Leu Pro
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 Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr Thr Thr Thr Pro
 1520 1525 1530
 Pro Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr Thr Thr Thr
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 Pro Pro Thr Ser Thr Thr Thr Leu Pro Pro Thr Thr Thr Thr Pro Ser
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 1745 1750 1755
 Thr Pro Leu Pro Pro Ser Ile Thr Pro Pro Thr Thr Thr Thr Thr
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 Ser Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr
 1775 1780 1785
 Thr Gly Trp Leu Asp Ser Gly Lys Pro Asn Phe His Lys Pro Gly
 1790 1795 1800
 Gly Asp Thr Glu Leu Ile Gly Asp Val Cys Gly Thr Thr Thr Thr
 1805 1810 1815

1805 1810 1815
Ala Asn Ile Ser Cys Arg Ala Thr Met Tyr Pro Asp Val Pro Ile
1820 1830
Gly Gln Leu Gly Gln Thr Val Val Cys Asp Val Ser Val Gly Leu
1835 1840 1845
Ile Cys Lys Asn Glu Asp Gln Lys Pro Gly Gly Val Ile Pro Met
1850 1855 1860
Ala Phe Cys Leu Asn Tyr Glu Ile Asn Val Gln Cys Cys Glu Cys
1865 1870 1875
Val Thr Gln Pro Thr Thr Met Thr Thr Thr Thr Thr Glu Asn Pro
1880 1885 1890
Thr Pro Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr
1895 1900 1905
Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro
1910 1915 1920
Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Thr Gly
1925 1930 1935
Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val
1940 1945 1950
Thr Pro Thr Pro Thr Thr Gly Thr Gln Thr Pro Thr Thr Thr
1955 1960 1965
Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Thr Thr
1970 1975 1980
Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr
1985 1990 1995
Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr
2000 2005 2010
Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro
2015 2020 2025
Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr
2030 2035 2040
Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr
2045 2050 2055
Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr
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Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Thr Thr Thr Thr Thr
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2105 2110 2115

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Thr Thr Thr Val Thr Pro Thr Pro Thr Gly Thr Thr Gln Thr
2135 2140 2145
Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Thr Val Thr Pro Thr
2150 2155 2160
Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr
2165 2170 2175
Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln
2180 2185 2190
Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro
2195 2200 2205
Thr Pro Thr Pro Thr Gly Thr Gln Thr Thr Thr Thr Thr Pro Ile
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2225 2230 2235
Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr
2240 2245 2250
Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Thr Thr Thr Thr Pro
2255 2260 2265
Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Thr Gly
2270 2275 2280
Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val
2285 2290 2295
Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Thr
2300 2305 2310
Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Thr
2315 2320 2325
Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr
2330 2335 2340
Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr
2345 2350 2355
Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro
2360 2365 2370
Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr
2375 2380 2385
Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr
2390 2395 2400
Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr
2405 2410 2415
Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Thr Thr Thr Thr Thr
2420 2425 2430

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Pro Thr	Pro Thr Pro Thr Thr Thr Thr	3290	3295	Thr Thr Thr Thr Thr	Thr Thr Thr	3300
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Pro Pro Pro Lys Pro Pro Arg Pro Gln Pro Pro Pro Gln Gln Val Arg
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Ser Ala Thr Ala Gly Ser Glu Gly Gly Phe Leu Ala Pro Glu Tyr Arg
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Glu Glu Gly Ala Ala Val Ala Ser Arg Val Arg Arg Arg Gly Gln Gln
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Asp Val Leu Arg Gly Pro Asn Val Cys Gly Ser Arg Phe His Ser Tyr
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Cys Cys Pro Gly Trp Lys Thr Leu Pro Gly Gly Asn Gln Cys Ile Val
100 105 110

Pro Ile Cys Arg Asn Ser Cys Gly Asp Gly Phe Cys Ser Arg Pro Asn
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Met Cys Thr Cys Ser Ser Gly Gln Ile Ser Ser Thr Cys Gly Ser Lys
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Ser Ile Gln Gln Cys Ser Val Arg Cys Met Asn Gly Gly Thr Cys Ala
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Gln Pro Cys Ala Cys Val Tyr Gly Phe Thr Gly Pro Gln Cys Glu Arg
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Asp Tyr Arg Thr Gly Pro Cys Phe Thr Gln Val Asn Asn Gln Met Cys
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Gln Gly Gln Leu Thr Gly Ile Val Cys Thr Lys Thr Leu Cys Cys Ala
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260 265 270

Cys Gln Asp Val Asp Glu Cys Gln Ala Ile Pro Gly Ile Cys Gln Gly
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Gly His Lys Gln Ser Glu Thr Thr Gln Lys Cys Glu Asp Ile Asp Glu
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Cys Ser Ile Ile Pro Gly Ile Cys Glu Thr Gly Glu Cys Ser Asn Thr

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 Ile Cys Lys Pro Gly Phe Val Leu Ala Pro Asn Gly Arg Tyr Cys Thr 655
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476

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477

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 Ala Asp Cys Ile Asn Ser Pro Gly Ser Tyr Arg Cys Glu Cys Ala 1865
 Ala Gly Phe Lys Leu Ser Pro Asn Gly Ala Cys Val Asp Arg Asn 1880
 Glu Cys Leu Glu Ile Pro Asn Val Cys Ser His Gly Leu Cys Val 1895
 Asp Leu Gln Gly Ser Tyr Gln Cys Ile Cys His Asn Gly Phe Lys 1910

Ala Ser Gln Asp Gln Thr Met Cys Met Asp Val Asp Glu Cys Glu 1925
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 Tyr Asn Cys Leu Cys Tyr Pro Gly Phe Glu Leu Thr His Asn Asn 1955
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 Ser Glu Pro Pro Leu Leu His Trp Gln Gly Pro Pro Glu Val Gly Ala
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 Ile Ala Gly Pro Arg Arg Arg Gly Ala Leu Gln Gly Ala Ala Ala
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 Ala Asp Arg Ala Pro Gly Ala Ala Arg Gly Gly Ser Arg Trp Arg
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 Thr Val Leu Leu Ala Ser Tyr Thr Ser His Gly Ala Asp Ala Asn Leu
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 Glu Ala Gly Asn Val Lys Glu Thr Arg Ala Ser Arg Ala Lys Arg Arg
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 Gly Gly Gly His Asp Ala Leu Lys Gly Pro Asn Val Cys Gly Ser
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 Arg Tyr Asn Ala Tyr Cys Cys Pro Gly Trp Lys Thr Leu Pro Gly Gly
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 Asn Gln Cys Ile Val Pro Ile Cys Arg His Ser Cys Gly Asp Gly Phe
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 Lys Gln Leu Cys Cys Ala Thr Val Gly Arg Ala Trp Gly His Pro Cys
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 Trp Ser Pro Gly Val Thr Val Ala Pro Glu Met Cys Pro Ile Arg Ala
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 Pro Val Asn Val Thr Asp Tyr Cys Gln Leu Val Arg Tyr Leu Cys Gln 580 585 590 595
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 Asn Ala Gly Phe His Val Thr Arg Asp Gly Lys Asn Cys Glu Asp Met 690 695 700
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 Asp Thr His Met Arg Ser Thr Cys Tyr Gly Tyr Tyr Lys Arg Gly Gln 785 790 795 800
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 Ala Ser Thr Glu Tyr Ala Phe Gly Glu Pro Cys Gln Pro Cys Pro Ala 820 825 830
 Gln Asn Ser Ala Glu Tyr Gln Ala Leu Cys Ser Ser Gly Pro Gly Met 835 840 845
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486

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 Ser Val Gly Ala Ala Trp Gly Thr Glu Glu Cys Glu Glu Cys Pro 1115 1120 1125
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487

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 1880 1885
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 1910 1915
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 1940 1945
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 1955 1960
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 1970 1975
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 1985 1990
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 2015 2020
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 Gly Gly Ala Ser Cys His Asn Thr Leu Gly Ser Tyr Lys Cys Met 2750

492

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 Cys Ser Asn Thr Glu Gly Gly Tyr Leu Cys Gly Cys Pro Pro Gly 2795
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493

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 Lys Asp Val Gly Arg Ile Val Ile Gly Leu Phe Gly Lys Val Val Pro 60
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 Lys Thr Val Glu Asn Phe Val Ala Leu Ala Thr Gly Glu Lys Gly Tyr 80
 65 70 75
 Gly Tyr Lys Gly Ser Lys Phe His Arg Val Ile Lys Asp Phe Met Ile 95
 85 90
 Gln Gly Gly Asp Ile Thr Thr Gly Asp Gly Thr Gly Val Ser Ile 110
 100 105

Tyr Gly Glu Thr Phe Pro Asp Glu Asn Phe Lys Leu Lys His Tyr Gly 125
 115 120
 Ile Gly Trp Val Ser Met Ala Asn Ala Gly Pro Asp Thr Asn Gly Ser 140
 130 135
 Gln Phe Phe Ile Thr Leu Thr Lys Pro Thr Trp Leu Asp Gly Lys His 160
 145 150 155
 Val Val Phe Gly Lys Val Ile Asp Gly Met Thr Val Val His Ser Ile 175
 165 170
 Glu Leu Gln Ala Thr Asp Gly His Asp Arg Pro Leu Thr Asn Cys Ser 190
 180 185
 Ile Ile Asn Ser Gly Lys Ile Asp Val Lys Thr Pro Phe Val Val Glu 205
 195 200
 Ile Ala Asp Trp 210
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 <211> 321
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 <213> Homo sapiens
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 Leu Pro Gly Glu Asp Trp Val Phe Val Ser Ser Lys Asp Ala Asp Leu 45
 35 40
 Thr Asp Thr Ala Gln Thr Arg Ala Leu Phe Glu Lys Val Gln Pro Thr 60
 50 55
 His Val Ile His Leu Ala Ala Met Val Gly Gly Leu Phe Arg Asn Ile 80
 65 70 75
 Lys Tyr Asn Leu Asp Phe Trp Arg Lys Asn Val His Met Asn Asp Asn 95
 85 90
 Val Leu His Ser Ala Phe Glu Val Gly Ala Arg Lys Val Val Ser Cys 110
 100 105
 Leu Ser Thr Cys Ile Phe Pro Asp Lys Thr Thr Tyr Pro Ile Asp Glu 125
 115 120
 Thr Met Ile His Asn Gly Pro Pro His Asn Ser Asn Phe Gly Tyr Ser 140
 130 135
 Tyr Ala Lys Arg Met Ile Asp Val Gln Asn Arg Ala Tyr Phe Gln Gln 160
 145 150 155
 Tyr Gly Cys Thr Phe Thr Ala Val Ile Pro Thr Asn Val Phe Gly Pro 175
 165 170
 His Asp Asn Phe Asn Ile Glu Asp Gly His Val Leu Pro Gly Leu Ile 190
 180 185

His Lys Val His Leu Ala Lys Ser Ser Gly Ser Ala Leu Thr Val Trp
195 200 205
Gly Thr Gly Asn Pro Arg Arg Gln Phe Ile Tyr Ser Leu Asp Leu Ala
210 215 220
Gln Leu Phe Ile Trp Val Leu Arg Glu Tyr Asn Glu Val Glu Pro Ile
225 230 235 240
Ile Leu Ser Val Gly Glu Glu Asp Glu Val Ser Ile Lys Glu Ala Ala
245 250 255
Glu Ala Val Val Glu Ala Met Asp Phe His Gly Glu Val Thr Phe Asp
260 265 270
Thr Thr Lys Ser Asp Gly Gln Phe Lys Lys Thr Ala Ser Asn Ser Lys
275 280 285
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305 310 315 320
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<212> PRT
<213> Homo sapiens
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Leu Ala Val His Lys Asp Glu Gly Ser Asp Pro Arg Arg Glu Thr Pro
35 40 45
Pro Gly Ala Asp Pro Arg Glu Tyr Cys Thr Ser Asp Arg Asp Ile Val
50 55 60
Glu Val Val Arg Thr Glu Tyr Val Tyr Thr Arg Pro Pro Trp Ser
65 70 75 80
Asp Thr Leu Pro Thr Ile His Val Val Thr Pro Thr Tyr Ser Arg Pro
85 90 95
Val Gln Lys Ala Glu Leu Thr Arg Met Ala Asn Thr Leu Leu His Val
100 105 110
Pro Asn Leu His Trp Leu Val Val Glu Asp Ala Pro Arg Arg Thr Pro
115 120 125
Leu Thr Ala Arg Leu Leu Arg Asp Thr Gly Leu Asn Tyr Thr His Leu
130 135 140
His Val Glu Thr Pro Arg Asn Tyr Lys Leu Arg Gly Asp Ala Arg Asp

145 150 155 160
Pro Arg Ile Pro Arg Gly Thr Met Gln Arg Asn Leu Ala Leu Arg Trp
165 170 175
Leu Arg Glu Thr Phe Pro Arg Asn Ser Ser Gln Pro Gly Val Val Tyr
180 185 190
Phe Ala Asp Asp Asn Thr Tyr Ser Leu Glu Leu Phe Glu Glu Met
195 200 205
Arg Ser Thr Arg Arg Val Ser Val Trp Pro Val Ala Phe Val Gly Gly
210 215 220
Leu Arg Tyr Glu Ala Pro Arg Val Asn Gly Ala Gly Lys Val Val Arg
225 230 235 240
Trp Lys Thr Val Phe Asp Pro His Arg Pro Phe Ala Ile Asp Met Ala
245 250 255
Gly Phe Ala Val Asn Leu Arg Leu Ile Leu Gln Arg Ser Gln Ala Tyr
260 265 270
Phe Lys Leu Arg Gly Val Lys Gly Tyr Gln Glu Ser Ser Leu Leu
275 280 285
Arg Glu Leu Val Thr Leu Asn Asp Leu Glu Pro Lys Ala Ala Asn Cys
290 295 300
Thr Lys Ile Leu Val Trp His Thr Arg Thr Glu Lys Pro Val Leu Val
305 310 315 320
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325 330
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Cys Leu Pro Pro Leu Arg Ala Ala Ala Glu Gln Leu Arg Gln Lys Asp
35 40 45
Leu Arg Ile Ser Gln Leu Gln Ala Glu Leu Arg Arg Pro Pro Ala
50 55 60
Pro Ala Gln Pro Pro Glu Pro Glu Ala Leu Pro Thr Ile Tyr Val Val
65 70 75 80
Thr Pro Thr Tyr Ala Arg Leu Val Gln Lys Ala Glu Leu Val Arg Leu
85 90 95
Ser Gln Thr Leu Ser Leu Val Pro Arg Leu His Trp Leu Leu Val Glu
100 105 110

Asp Ala Glu Gly Pro Thr Pro Leu Val Ser Gly Leu Leu Ala Ala Ser
 115 120 125
 Gly Leu Leu Phe Thr His Leu Val Val Leu Thr Pro Lys Ala Gln Arg
 130 135 140
 Leu Arg Glu Gly Glu Pro Gly Trp Val His Pro Arg Gly Val Glu Gln
 145 150 155 160
 Arg Asn Lys Ala Leu Asp Trp Leu Arg Gly Arg Gly Ala Val Gly
 165 170 175
 Gly Glu Lys Asp Pro Pro Pro Gly Thr Gln Gly Val Val Tyr Phe
 180 185 190
 Ala Asp Asp Asp Asn Thr Tyr Ser Arg Glu Leu Phe Glu Glu Met Arg
 195 200 205
 Trp Thr Arg Gly Val Ser Val Trp Pro Val Gly Leu Val Gly Gly Leu
 210 215 220
 Arg Phe Glu Gly Pro Gln Val Gln Asp Gly Arg Val Val Gly Phe His
 225 230 235 240
 Thr Ala Trp Glu Pro Ser Arg Pro Phe Pro Val Asp Met Ala Gly Phe
 245 250 255
 Ala Val Ala Leu Pro Leu Leu Asp Lys Pro Asn Ala Gln Phe Asp
 260 265 270
 Ser Thr Ala Pro Arg Gly His Leu Glu Ser Ser Leu Leu Ser His Leu
 275 280 285
 Val Asp Pro Lys Asp Leu Glu Pro Arg Ala Ala Asn Cys Thr Arg Val
 290 295 300
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 35 40 45
 Gly Gly Tyr Glu Thr Cys Pro Thr Val Gln Pro Asn Met Leu Asn Val
 50 55 60
 His Leu Leu Pro His Thr His Asp Asp Val Gly Trp Leu Lys Thr Val
 65 70 75 80

Asp Gln Tyr Phe Tyr Gly Ile Lys Asn Asp Ile Gln His Ala Gly Val
 85 90 95
 Gln Tyr Ile Leu Asp Ser Val Ile Ser Ala Leu Leu Ala Asp Pro Thr
 100 105 110
 Arg Arg Phe Ile Tyr Val Glu Ile Ala Phe Phe Ser Arg Trp Trp His
 115 120 125
 Gln Gln Thr Asn Ala Thr Gln Glu Val Val Arg Asp Leu Val Arg Gln
 130 135 140
 Gly Arg Leu Glu Phe Ala Asn Gly Gly Trp Val Met Asn Asp Glu Ala
 145 150 155 160
 Ala Thr His Tyr Gly Ala Ile Val Asp Gln Met Thr Leu Gly Leu Arg
 165 170 175
 Phe Leu Glu Asp Thr Phe Gly Asn Asp Gly Arg Pro Arg Val Ala Trp
 180 185 190
 His Ile Asp Pro Phe Gly His Ser Arg Glu Gln Ala Ser Leu Phe Ala
 195 200 205
 Gln Met Gly Phe Asp Gly Phe Phe Gly Arg Leu Asp Tyr Gln Asp
 210 215 220
 Lys Trp Val Arg Met Gln Lys Leu Glu Met Glu Gln Val Trp Arg Ala
 225 230 235 240
 Ser Thr Ser Leu Lys Pro Pro Thr Ala Asp Leu Phe Thr Gly Val Leu
 245 250 255
 Pro Asn Gly Tyr Asn Pro Pro Arg Asn Leu Cys Trp Asp Val Leu Cys
 260 265 270
 Val Asp Gln Pro Leu Val Glu Asp Pro Arg Ser Pro Glu Tyr Asn Ala
 275 280 285
 Lys Glu Leu Val Asp Tyr Phe Leu Asn Val Ala Thr Ala Gln Gly Arg
 290 295 300
 Tyr Tyr Arg Thr Asn His Thr Val Met Thr Met Gly Ser Asp Phe Gln
 305 310 315 320
 Tyr Glu Asn Ala Asn Met Trp Phe Lys Asn Leu Asp Lys Leu Ile Arg
 325 330 335
 Leu Val Asn Ala Gln Gln Ala Lys Gly Ser Ser Val His Val Leu Tyr
 340 345 350
 Ser Thr Pro Ala Cys Tyr Leu Trp Glu Leu Asn Lys Ala Asn Leu Thr
 355 360 365
 Trp Ser Val Lys His Asp Asp Phe Phe Pro Tyr Ala Asp Gly Pro His
 370 375 380
 Gln Phe Trp Thr Gly Tyr Phe Ser Ser Arg Pro Ala Leu Lys Arg Tyr
 385 390 395 400
 Glu Arg Leu Ser Tyr Asn Phe Leu Gln Val Cys Asn Gln Leu Glu Ala

405 410 415
 Leu Val Gly Leu Ala Ala Asn Val Gly Pro Tyr Gly Ser Gly Asp Ser 430
 420 425
 Ala Pro Leu Asn Glu Ala Met Ala Val Leu Gln His His Asp Ala Val 445
 435 440
 Ser Gly Thr Ser Arg Gln His Val Ala Asn Asp Tyr Ala Arg Gln Leu 460
 450 455
 Ala Ala Gly Trp Gly Pro Cys Glu Val Leu Leu Ser Asn Ala Leu Ala 480
 465 475
 Arg Leu Arg Gly Phe Lys Asp His Phe Thr Phe Cys Gln Gln Leu Asn 495
 485 490
 Ile Ser Ile Cys Pro Leu Ser Gln Thr Ala Ala Arg Phe Gln Val Ile 510
 500 505
 Val Tyr Asn Pro Leu Gly Arg Lys Val Asn Trp Met Val Arg Leu Pro 525
 515 520
 Val Ser Glu Gly Val Phe Val Val Lys Asp Pro Asn Gly Arg Thr Val 540
 530 535
 Pro Ser Asp Val Val Ile Phe Pro Ser Ser Asp Ser Gln Ala His Pro 560
 545 550 555
 Pro Glu Leu Leu Phe Ser Ala Ser Leu Pro Ala Leu Gly Phe Ser Thr 575
 565 570
 Tyr Ser Val Ala Gln Val Pro Arg Trp Lys Pro Gln Ala Arg Ala Pro 590
 580 585
 Gln Pro Ile Pro Arg Arg Ser Trp Ser Pro Ala Leu Thr Ile Glu Asn 605
 595 600
 Glu His Ile Arg Ala Thr Phe Asp Pro Asp Thr Gly Leu Leu Met Glu 620
 610 615
 Ile Met Asn Met Asn Gln Gln Leu Leu Leu Pro Val Arg Gln Thr Phe 640
 625 630 635
 Phe Trp Tyr Asn Ala Ser Ile Gly Asp Asn Glu Ser Asp Gln Ala Ser 655
 645 650
 Gly Ala Tyr Ile Phe Arg Pro Asn Gln Gln Lys Pro Leu Pro Val Ser 670
 660 665
 Arg Trp Ala Gln Ile His Leu Val Lys Thr Pro Leu Val Gln Glu Val 685
 675 680
 His Gln Asn Phe Ser Ala Trp Cys Ser Gln Val Val Arg Leu Tyr Pro 700
 690 695
 Gly Gln Arg His Leu Glu Leu Glu Trp Ser Val Gly Pro Ile Pro Val 720
 705 710 715
 Gly Asp Thr Trp Gly Lys Glu Val Ile Ser Arg Phe Asp Thr Pro Leu 735
 725 730

500

Glu Thr Lys Gly Arg Phe Tyr Thr Asp Ser Asn Gly Arg Glu Ile Leu 740
 745 750
 Glu Arg Arg Arg Asp Tyr Arg Pro Thr Trp Lys Leu Asn Gln Thr Glu 765
 755 760
 Pro Val Ala Gly Asn Tyr Tyr Pro Val Asn Thr Arg Ile Tyr Ile Thr 780
 770 775
 Asp Gly Asn Met Gln Leu Thr Val Leu Thr Asp Arg Ser Gln Gly Gly 800
 785 790 795
 Ser Ser Leu Arg Asp Gly Ser Leu Glu Leu Met Val His Arg Arg Leu 815
 805 810
 Leu Lys Asp Asp Gly Arg Gly Val Ser Glu Pro Leu Met Glu Asn Gly 830
 820 825
 Ser Gly Ala Trp Val Arg Gly Arg His Leu Val Leu Leu Asp Thr Ala 845
 835 840
 Gln Ala Ala Ala Ala Gly His Arg Leu Leu Ala Glu Gln Glu Val Leu 860
 850 855
 Ala Pro Gln Val Val Leu Ala Pro Gly Gly Gly Ala Ala Tyr Asn Leu 880
 865 870 875
 Gly Ala Pro Pro Arg Thr Gln Phe Ser Gly Leu Arg Arg Asp Leu Pro 895
 885 890
 Pro Ser Val His Leu Leu Thr Leu Ala Ser Trp Gly Pro Glu Met Val 910
 900 905
 Leu Leu Arg Leu Glu His Gln Phe Ala Val Gly Glu Asp Ser Gly Arg 925
 915 920
 Asn Leu Ser Ala Pro Val Thr Leu Asn Leu Arg Asp Leu Phe Ser Thr 940
 930 935
 Phe Thr Ile Thr Arg Leu Gln Glu Thr Thr Leu Val Ala Asn Gln Leu 960
 945 950 955
 Arg Glu Ala Ala Ser Arg Leu Lys Trp Thr Thr Asn Thr Gly Pro Thr 975
 965 970
 Pro His Gln Thr Pro Tyr Gln Leu Asp Pro Ala Asn Ile Thr Leu Glu 990
 980 985
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 995 1000
 Asp Gly 1010
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 <213> Homo sapiens
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501

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35 40
Gly Gly Gly Gly Pro Gly Gln Gly Phe Asp Val Ala Lys Thr Gly Asp 60
50 55
Ala Arg Ile Gly Phe Val Gly Phe Pro Ser Val Gly Lys Ser Thr Leu 80
65 70 75
Leu Ser Asn Leu Ala Gly Val Tyr Ser Gln Val Ala Ala Tyr Gln Phe 95
85
Thr Thr Thr Thr Val Pro Gly Val Ile Arg Tyr Lys Gly Ala Lys 110
100 105
Ile Gln Leu Leu Asp Leu Pro Gly Ile Ile Gln Gly Ala Lys Asp Gly 125
115 120
Lys Gly Arg Gly Arg Gln Val Ile Ala Val Ala Arg Thr Cys Asn Leu 140
130 135
Ile Leu Ile Val Leu Asp Val Leu Lys Pro Leu Gly His Lys Lys Ile 160
145 150 155
Ile Gln Asn Gln Leu Gln Gly Phe Gly Ile Arg Leu Asn Ser Lys Pro 175
165 170
Pro Asn Ile Gly Phe Lys Lys Lys Asp Lys Gly Gly Ile Asn Leu Thr 190
180 185
Ala Thr Cys Pro Gln Ser Gln Leu Asp Ala Gln Thr Val Lys Ser Ile 205
195 200
Leu Ala Gln Tyr Lys Ile His Asn Ala Asp Val Thr Leu Arg Ser Asp 220
210 215
Ala Thr Ala Asp Asp Leu Ile Asp Val Val Gln Gly Asn Arg Val Tyr 240
225 230 235
Ile Pro Cys Ile Tyr Val Leu Asn Lys Ile Asp Gln Ile Ser Ile Gln 255
245 250
Glu Leu Asp Ile Ile Tyr Lys Val Pro His Cys Val Pro Ile Ser Ala 270
260 265
His His Arg Trp Asn Phe Asp Asp Leu Leu Gln Lys Ile Trp Asp Tyr 285
275 280
Leu Lys Leu Val Arg Ile Tyr Thr Lys Pro Lys Gly Gln Leu Pro Asp 300
290 295
Tyr Thr Ser Pro Val Val Leu Pro Tyr Ser Arg Thr Thr Val Gln Asp 320
305 310 315
Phe Cys Met Lys Ile His Lys Asn Leu Ile Lys Gln Phe Lys Tyr Ala 335
325 330
Leu Val Trp Gly Leu Ser Val Lys His Asn Pro Gln Lys Val Gly Lys

Asp His Thr Leu Gln Asp Gln Asp Val Ile Gln Ile Val Lys Lys 365
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Lys Leu Ala Lys Tyr Arg Ala Gln Leu Leu Gln Pro Ser Lys Ser Ala 45
35 40
Ser Ser Lys Gly Gln Gly Phe Asp Val Met Lys Ser Gly Asp Ala Arg 60
50 55
Val Ala Leu Ile Gly Phe Pro Ser Val Gly Lys Ser Thr Phe Leu Ser 80
65 70 75
Leu Met Thr Ser Thr Ala Ser Gln Ala Ala Ser Tyr Gln Phe Thr Thr 95
85 90
Leu Thr Cys Ile Pro Gly Val Ile Gln Tyr Lys Gly Ala Asn Ile Gln 110
100 105
Leu Leu Asp Leu Pro Gly Ile Ile Gln Gly Ala Ala Gln Gly Lys Gly 125
115 120
Arg Gly Arg Gln Val Ile Ala Val Ala Arg Thr Ala Asp Val Ile Ile 140
130 135
Met Met Leu Asp Ala Thr Lys Gly Gln Val Gln Arg Ser Leu Leu Gln 160
145 150 155
Lys Gln Leu Gln Ser Val Gly Ile Arg Leu Asn Lys His Lys Pro Asn 175
165 170
Ile Tyr Phe Lys Pro Lys Lys Gly Gly Ile Ser Phe Asn Ser Thr 190
180 185
Val Thr Leu Thr Gln Cys Ser Gln Lys Leu Val Gln Leu Ile Leu His 205
195 200
Glu Tyr Lys Ile Phe Asn Ala Gln Val Leu Phe Arg Gln Asp Cys Ser 220
210 215
Pro Asp Gln Phe Ile Asp Val Ile Val Gly Asn Arg Val Tyr Met Pro 240
225 230 235
Cys Leu Tyr Val Tyr Asn Lys Ile Asp Gln Ile Ser Met Gln Gln Val 255
245 250
Asp Arg Leu Ala Arg Lys Pro Asn Ser Val Ile Ser Cys Gly Met 270
260 265

Lys Leu Asn Leu Asp Tyr Leu Leu Glu Met Leu Trp Glu Tyr Leu Ala 285
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 Leu Thr Cys Ile Tyr Thr Lys Arg Gly Gln Arg Pro Asp Phe Thr 300
 290
 Asp Ala Ile Ile Leu Arg Lys Gly Ala Ser Val Glu His Val Cys His 320
 305 310 315
 Arg Ile His Arg Ser Leu Ala Ser Gln Phe Lys Tyr Ala Leu Val Trp 335
 325 330
 Gly Thr Ser Thr Lys Tyr Ser Pro Gln Arg Val Gly Leu Thr His Thr 350
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 Met Glu His Glu Asp Val Ile Gln Ile Val Lys Lys 360
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 35 40
 Thr Thr Val Arg Thr Gly Leu Asp Leu Lys Ala Asn Lys Thr Phe Ala 60
 50 55
 Tyr His Lys Asp Met Pro Leu Ile Phe Ile Gly Gly Val Pro Arg Ser 80
 65 70 75
 Gly Thr Thr Leu Met Arg Ala Met Leu Asp Ala His Pro Asp Ile Arg 95
 85 90
 Cys Gly Glu Thr Arg Val Ile Pro Arg Ile Leu Ala Leu Lys Gln 110
 100 105
 Met Trp Ser Arg Ser Ser Lys Glu Lys Ile Arg Leu Asp Glu Ala Gly 125
 115 120
 Val Thr Asp Glu Val Leu Asp Ser Ala Met Gln Ala Phe Leu Leu Glu 140
 130 135
 Ile Ile Val Lys His Gly Glu Pro Ala Pro Tyr Leu Cys Asn Lys Asp 160
 145 150 155
 Pro Phe Ala Leu Lys Ser Leu Thr Tyr Leu Ser Arg Leu Phe Pro Asn 175
 165 170
 Ala Lys Phe Leu Leu Met Val Arg Asp Gly Arg Ala Ser Val His Ser 190
 180 185
 Met Ile Ser Arg Lys Val Thr Ile Ala Gly Phe Asp Leu Asn Ser Tyr 205
 195 200

504

Arg Asp Cys Leu Thr Lys Trp Asn Arg Ala Ile Glu Thr Met Tyr Asn 220
 210 215
 Gln Cys Met Glu Val Gly Tyr Lys Lys Cys Met Leu Val His Tyr Glu 240
 225 230 235
 Gln Leu Val Leu His Pro Glu Arg Trp Met Arg Thr Leu Leu Lys Phe 255
 245 250
 Leu Gln Ile Pro Trp Asn His Ser Val Leu His His Glu Glu Met Ile 270
 260 265
 Gly Lys Ala Gly Gly Val Ser Leu Ser Lys Val Glu Arg Ser Thr Asp 285
 275 280
 Gln Val Ile Lys Pro Val Asn Val Gly Ala Leu Ser Lys Trp Val Gly 300
 290 295
 Lys Ile Pro Pro Asp Val Leu Gln Asp Met Ala Val Ile Ala Pro Met 320
 305 310 315
 Leu Ala Lys Leu Gly Tyr Asp Pro Tyr Ala Asn Pro Pro Asn Tyr Gly 335
 325 330
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 Val Glu 370
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 35 40
 Gln Glu Glu Leu Val Met Val Gly Thr Asn His Val Glu Tyr Arg Tyr 60
 50 55
 Gly Lys Ala Met Pro Leu Ile Phe Val Gly Gly Val Pro Arg Ser Gly 80
 65 70 75
 Thr Thr Leu Met Arg Ala Met Leu Asp Ala His Pro Glu Val Arg Cys 95
 85 90
 Gly Glu Thr Arg Ile Ile Pro Arg Val Leu Ala Met Arg Gln Ala 110
 100 105
 Trp Ser Lys Ser Gly Arg Glu Lys Leu Arg Leu Asp Glu Ala Gly Val 115
 120

505

115 120 125
 Thr Asp Glu Val Leu Asp Ala Ala Met Gln Ala Phe Ile Leu Glu Val
 130 135 140
 Ile Ala Lys His Gly Glu Pro Ala Arg Val Leu Cys Asn Lys Asp Pro
 145 150 155 160
 Phe Thr Leu Lys Ser Ser Val Tyr Leu Ser Arg Leu Phe Pro Asn Ser
 165 170 175
 Lys Phe Leu Leu Met Val Arg Asp Gly Arg Ala Ser Val His Ser Met
 180 185 190
 Ile Thr Arg Lys Val Thr Ile Ala Gly Phe Asp Leu Ser Ser Tyr Arg
 195 200 205
 Asp Cys Leu Thr Lys Trp Asn Lys Ala Ile Glu Val Met Tyr Ala Gln
 210 215 220
 Cys Met Glu Val Gly Lys Glu Lys Cys Leu Pro Val Tyr Tyr Glu Gln
 225 230 235 240
 Leu Val Leu His Pro Arg Arg Ser Leu Lys Leu Ile Leu Asp Phe Leu
 245 250 255
 Gly Ile Ala Trp Ser Asp Ala Val Leu His His Glu Asp Leu Ile Gly
 260 265 270
 Lys Pro Gly Gly Val Ser Leu Ser Lys Ile Glu Arg Ser Thr Asp Gln
 275 280 285
 Val Ile Lys Pro Val Asn Leu Glu Ala Leu Ser Lys Trp Thr Gly His
 290 295 300
 Ile Pro Gly Asp Val Val Arg Asp Met Ala Gln Ile Ala Pro Met Leu
 305 310 315 320
 Ala Gln Leu Gly Tyr Asp Pro Tyr Ala Asn Pro Pro Asn Tyr Gly Asn
 325 330 335
 Pro Asp Pro Phe Val Ile Asn Asn Thr Gln Arg Val Leu Lys Gly Asp
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 aagtagata ataactac gaagcccg cgtctctct ccttgcctt gaggcagct
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 120
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 240
 300
 360

506

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INTERNATIONAL SEARCH REPORT

International application No. PCT/US02/17382	
A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : C12Q 1/00, 1/68; G01N 33/53; A61K 49/00 US CL : 435/4, 6, 7, 1; 424/9, 1 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/4, 6, 7, 1; 424/9, 1	
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched	
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) WEST, MEDLINE	
C. DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No.
A	US 6,020,135 A (LEVINE et al) 27 March 1998 (27.03.1998) 1-25
A	WO 00/31530 A2 (THE GOVERNMENT OF THE UNITED STATES OF AMERICA REPRESENTED BY THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES) 02 June 2000 (02.06.2000). 1-25
A	US 5,908,730 A (REED et al) 01 June 1999 (01.06.1999) 1-25
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex. * Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "B" earlier application or patent published on or after the international filing date "C" document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (to be specified) "D" document referring to an oral disclosure, use, exhibition or other means "E" document published prior to the international filing date but later than the priority date claimed "F" document published after the international filing date or priority date and not to conflict with the application but cited to understate the principle or theory underlying the invention "G" document of particular relevance: the cited invention cannot be considered novel or cannot be considered to involve an inventive step unless the document is taken alone "H" document of particular relevance: the cited invention cannot be considered to involve an inventive step unless the document is combined with one or more other documents, each contribution being obvious to a person skilled in the art "I" document neither of the same piece family	
Date of the actual completion of the international search 19 September 2002 (19.09.2002) Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20531 Facsimile No. (703)305-5130 Telephone No. 703-308-0196	
Date of mailing of the international search report 18 OCT 2002 Authorized officer Gary B. Haines Telephone No. 703-308-0196	

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